ACCESS TO MEDICINES IN INDIA

EDITORS

Sakthivel Selvaraj • Dinesh Abrol • K.M. Gopakumar

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CONTENTS

List of Tables and Figures

Tables

Figures

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Finally, any omissions and commissions, found in this monograph are entirely due to authors' and not attributed to the organisations they belong to.

1

SAKTHIVEL SELVARAJ

The Indian Health System

Current Trends and Patterns

Introduction

India's current system of health care delivery and financing is predominantly private in nature. Nearly 80 per cent of all outpatient care and 60 per cent of all hospital care delivery occurs at private health facilities. Nearly 70 per cent of all health care financing comes from private out-of-pocket spending. However, the regulatory structure and especially the enforcement of regulatory mechanisms are considered poor and weak. It is in this background that this chapter deals with some of the key elements of the Indian health system, including the health outcomes indicators.

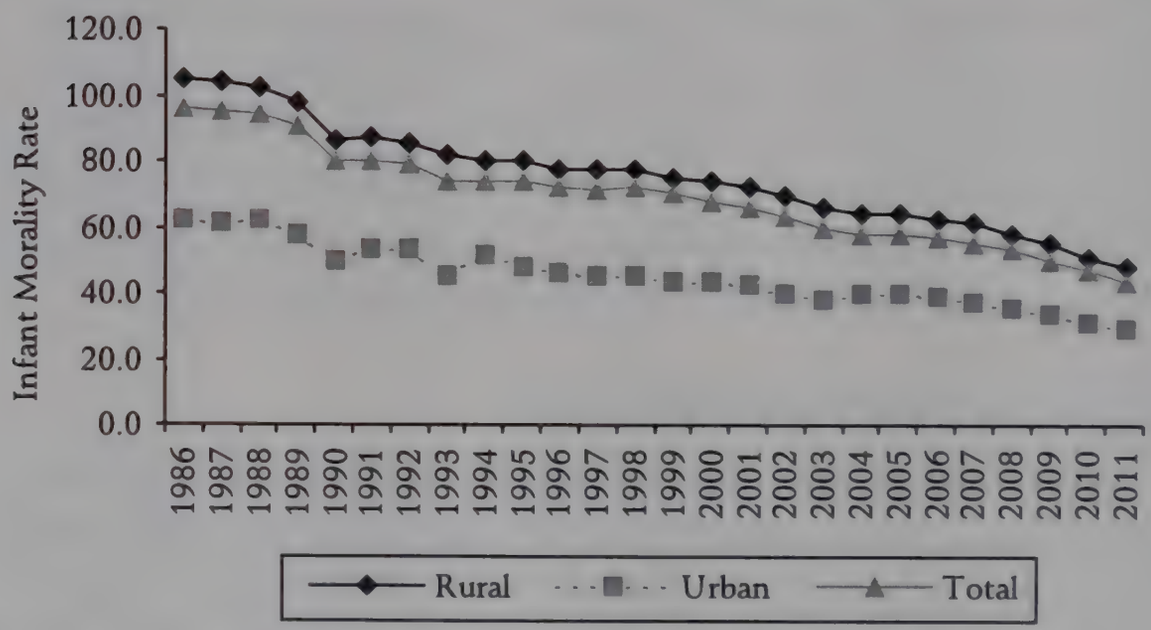
India's Current Key Health Outcomes

India is one of the major emerging economies, with a sustained annual growth rate of over 5.5-6.0 per cent for the past three decades. India is often compared with China in terms of economic growth. However, its human development record has been rather dismal compared to China and to other low- and middle-income countries (LMICs). India's infant mortality rate (IMR), maternal mortality rate (MMR), immunisation rates etc. are considered to be among the worst, with some indicators falling behind those of sub-Saharan African (SSA) countries. India is far off-track in relation to achieving the Millennium Development Goal (MDG) targets of reducing IMR to 28, child mortality to 42 and MMR to 109 by the year 2015.

According to recent Sample Registration System (SRS) estimates (2011),[1] India's IMR currently stands at 44 per thousand live births, with baby girls registering a higher rate of 46 as against baby boys at 43. India's IMR was around 72 in 1998, which declined to about 58 in 2005 and 44 in 2011 (Figure 1.1). Despite best efforts to reduce IMR and MMR through the Safe Motherhood Scheme (Janani Suraksha Yojana—JSY) under the National Rural Health Mission (NRHM), the decline in IMR has been rather gradual in the last 10 years, with no clear trends of a sharp decline in the post-JSY phase. This is true of both rural and urban areas. Rural India recorded an IMR of 77 per 1,000 live births as against urban India's 45 per 1,000 live births in 1998. In 2011, the respective IMRs were 48 and 29 in rural and urban India (Figure 1.1).

Figure 1.1

Trends in Infant Mortality Rates per 1,000 Live Births in India, 1986-2011



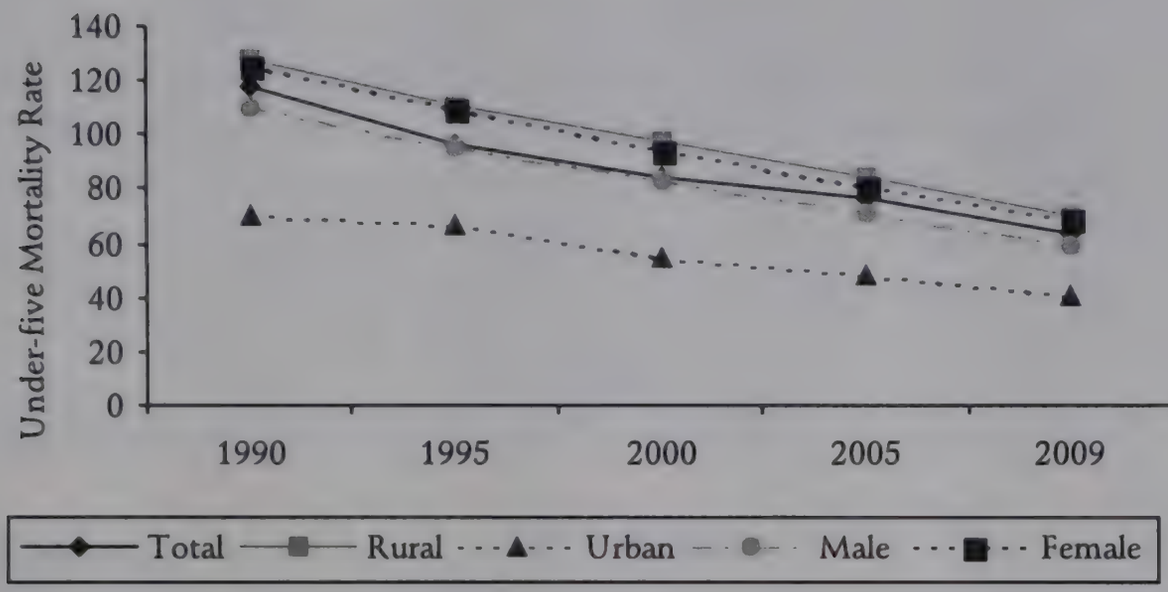
Source: Respective SRS Bulletin, Registrar General, Government of India.

Similarly, there exists significant variation in Under-five mortality between urban and rural India. Rural India recorded an under-five mortality rate of 111 per 1000 live births as against urban India's 67 per 1000 live births during 1995. In 2009, the respective under-five mortality rate was 71 and 41 in Rural and Urban India (see Figure 1.2).

1. Office of the Registrar General of India, Sample Registration System.

Figure 1.2

Trends in Under-Five Mortality



Source: Respective SRS Bulletin, Registrar General, Government of India.

With regard to MMR, India has been lagging far behind the MDG target and is unlikely to achieve it by 2015. India's MMR (measured by number of women aged 15-49 years dying due to maternal causes per 100,000 live births) has registered a gradual decline from 327 during 1999-2001 to 212 during 2007-2009, a 35 per cent decline in the last 10 years. During the same period, the southern states' average MMR went down from 206 to 127, while the Empowered Action Group (EAG)[2] states and Assam witnessed a sharp decline from 461 to 308 (Figure 1.3). Individual states such as Tamil Nadu, Kerala and Maharashtra have already realised the MDG target of 109, while Andhra Pradesh, West Bengal, Gujarat and Haryana are in close range of achieving the target (SRS, 2011).

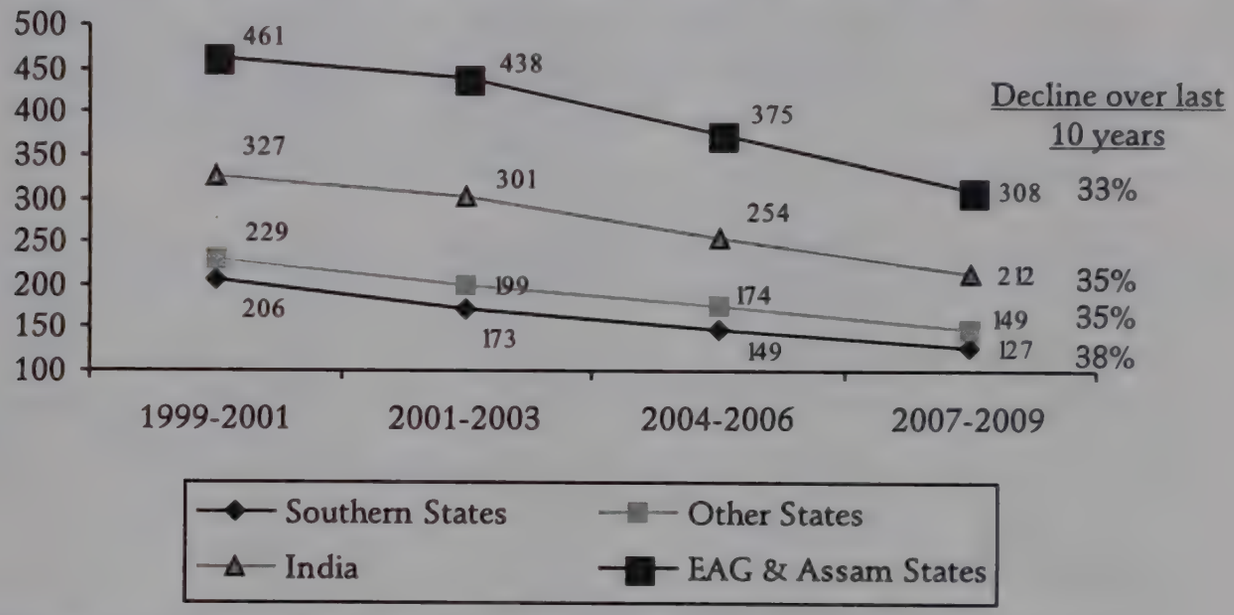
Immunisation is another critical health indicator due to its role in averting disability and disease. In India, the primary immunisation schedule is expected to be covered for every child by the time he/she turns 12 months old. This is expected to include one dose of BCG, three injections of DPT, three doses of polio and one injection of measles vaccines. Figure 1.4 reveals that only about 61 per cent of all Indian children aged 12-23 months are fully immunised. In fact, the coverage is low in rural areas at 58.5 per

2. EAG states are those whose health status indicators, including IMR, MMR are relatively worse than the other Indian states. There are 8 EAG states in India under the current policy intervention through National Rural Health Mission (now rechristened as National Health Mission).

cent in comparison to urban India's average of 67.4 per cent. It is estimated that approximately 8 per cent of the children failed to receive even a single dose of vaccine (UNICEF, 2009). At nearly 87 per cent, the BCG vaccination coverage appears to be the highest among all vaccinations, with the Hepatitis B vaccination coverage, for example, at only around 59 per cent. Although India now claims that the country is polio-free, only about 70 per cent of all children received all three doses of the polio vaccine (OPV).

Figure 1.3

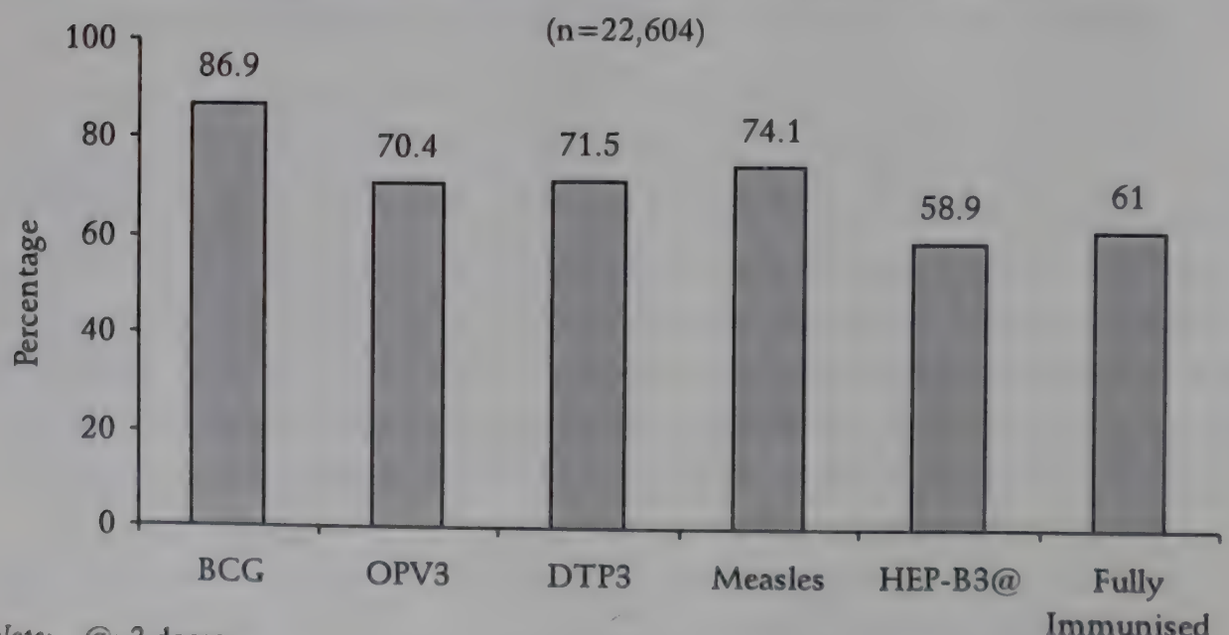
Trends and Patterns in the Maternal Mortality Rate in India, 1999-2009



Source: Respective SRS Bulletin, Registrar General, Government of India

Figure 1.4

Immunisation among Children Aged 12-23 Months (in Percentage)



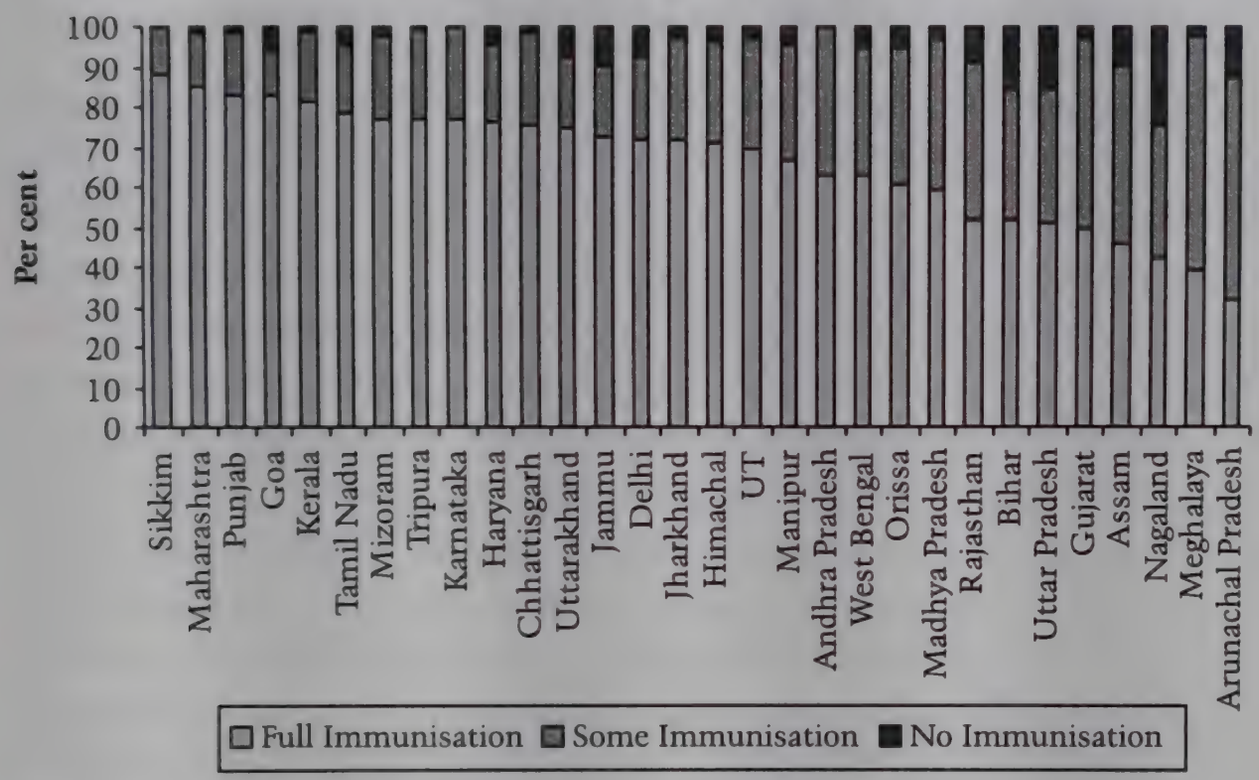
Note: @: 3 doses

Source: UNICEF (2009). *Coverage Evaluation Survey: All India Report.*

India's record of 61 per cent full immunisation coverage masks great variation between states (Figure 1.5). The disparity in coverage is strikingly stark as Uttar Pradesh, for instance, covered barely 40 per cent of children with full immunisation record. Bihar and Madhya Pradesh have slightly higher levels than Uttar Pradesh, but their full immunisation coverage is still less than 50 per cent. There are about nine states whose full immunisation coverage is less than the national average. Among the bigger states, some of the leading states in full immunisation coverage are: Punjab, Kerala, Maharashtra, Tamil Nadu and Himachal Pradesh, whose average is close to 80 per cent and above.

Figure 1.5

Immunisation Status among Children Aged 12-23 Months in Indian States



Source: UNICEF (2009). *Coverage Evaluation Survey: All India Report.*

India is presently experiencing a "double burden of disease". The incidence of several preventable infectious diseases is rising sharply, while non-communicable diseases are witnessing a disturbing upward trend. However, India's heterogeneous health care system that is dominated by the private care sector is threatening to sharpen the divide, as health care costs are skyrocketing. Sustained underinvestment leading to lack of infrastructure and deterioration in public health care infrastructure has been a serious concern. In view of these poor policies, access and affordability of health

care has suffered enormously, leading to India's failure to achieve good health standards and provide financial risk protection to the population in general and the poor in particular.

Despite the avowed intentions of strengthening the public health system and providing focus on primary health care, the dominance of the private sector is felt in almost every sphere of the health system—financing, provision, medical education and training, medical technology and diagnostics, manufacture and sale of medicines, etc. The reach and diversity of the private health care sector demonstrates the stark contrast within the system. The private sector encompasses all and sundry from for-profit large corporate entities to not-for-profit trusts (private and religious), from general practitioners and qualified specialists to unqualified rural medical practitioners, etc.

Underinvestment by the government and neglect of public provision of health services in the past has led to the emergence of dominant but unregulated and unqualified private providers. Evidence from nationally representative large-scale household surveys in the last two decades shows a sharp increase in the role of private health care provision. The private sector not only dominates but continues to consolidate its share of health care delivery in outpatient care involving largely general practitioners (including allopathy and non-allopathy providers) and pharmacists. Nearly 80 per cent of all outpatient care in India is now provided by the private sector, with a considerable increase in its share over the last two decades. The government's inability to finance and provide care in the last two decades is clearly demonstrated in the hospitalisation cover to the population. There has been a sharp reduction in the provision of government inpatient care and a concomitant rise of private provision from about 40 per cent in 1986-87 to around 60 per cent in 2004 (Selvaraj and Karan, 2009).

Further evidence from informal facility surveys of the National Sample Survey (NSS) shows that there were an estimated 1.3 million private health care provider facilities employing about 2.2 million workers during 2006-07. The evidence indicates that over one-third of them have no registration of any kind and 25 per

cent are AYUSH (Indian system of medicines including Ayurveda, Unani, Siddha and Homeopathy) practitioners. The heterogeneity of India's private health care sector can be further demonstrated by its large number of informal providers—quacks (almost one in every village), bonesetters, traditional healers, traditional birth attendants (TBAs) etc.

The presence of a large and unregulated private sector has implications for cost, quality and quantity. For example, Rao *et al.* (2005: 91) noted that "in a survey of 24 hospitals in Mumbai, half were found to be operating from sheds and lofts, congested spaces, with leaking operation theatres (OTs) and over 90 per cent of unqualified nurses and doctors with degrees in alternative medicine providing care in allopathic medicine," an ethically and legally prohibited practice. Private care is characterised by unnecessary diagnostic tests, repeated consultation and superfluous surgery, without providing any information on diagnosis or treatment, a reflection of supply-side moral hazard.

It is often argued that fast-expanding private providers can fill the gaps created by declining government participation in the health sector. However, apart from the concern over quality, there remains a serious concern related to affordability of and access to private health care providers. This has repercussions for equity of and access to health care services. Compelling evidence indicates that although the proportion of non-treated ailments has remained largely constant over the years, among the reasons behind absence of formal treatment, factors such as unavailability of health care services and high costs of treatment have been on the rise in the last two decades. While inaccessibility of medical facilities was the reason for non-treatment in a little over 12 per cent of cases in rural areas of the country in 2004, financial reasons accounted for well over one-fourth of the cases of untreated ailments. The latter's proportion was only 15 per cent in 1986-87, indicating a deterioration in access of poor people to government-run subsidised health care facilities in rural areas. In urban areas too, the rising financial burden of paying for over-heated private health care was responsible for one-fifth of cases of non-treatment in 2004, as against only 10 per cent in 1986-87 (Selvaraj and Karan, 2009).

An ever more sizeable share of untreated ailments in recent years is due to runaway health care costs in the largely unregulated private sector, in addition to financial barriers caused by user fees in public facilities. Further, households seeking care in public hospitals are increasingly asked to buy expensive drugs and diagnostics from private outlets on the grounds that these facilities are unavailable in the public units.

It is in this background that the Indian government launched the National Rural Health Mission (NRHM) in 2005. Attempting to integrate all the erstwhile vertical programmes, the NRHM introduced innovative ways of flexible funding into the health care system and focused on the Safe Motherhood Scheme. Since the initiation of the programme, maternal and child mortality rates have declined gradually. However, these figures remain unimpressive for a country at India's income level. Interestingly, the financial incentive programme associated with the Safe Motherhood Scheme appears to have had a salutary impact, as institutional deliveries increased dramatically from about 40 per cent in 2005-06 to almost 79 per cent in 2008-09.

Inequity in Consumption of Health Services

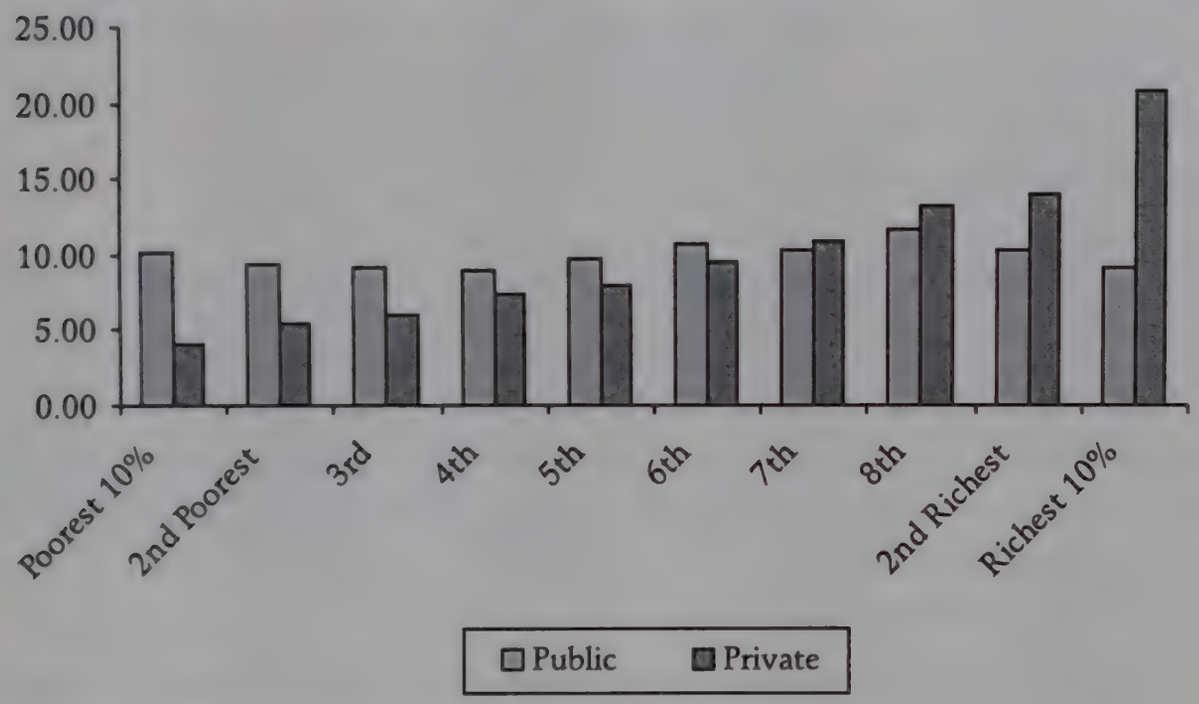
India's poor health outcomes are also marked by large-scale inequity in access to health care delivery. Economically and socially vulnerable groups not only are denied care due to physical and financial barriers, those who seek health care are also discriminated against. As mentioned above, in 2004, nearly 30 per cent of cases in rural India of those who were ill but did not seek care, and 20 per cent in urban India, were attributed to the financial barrier. Socially backward groups tend to suffer greater impoverishment due to out-of-pocket spending on health care (Balarajan *et al.*, 2011)

Past evidence demonstrated that in earlier decades the richest groups ended up accounting for a larger share of public health subsidies. But that trend appears to have reversed in the last decade or so. This is not due to pro-poor planning and policies of the government but as the role of the private sector has increased manifold, affluent sections of society have tended to use the

mushrooming private corporate health care facilities. The Benefit-Incidence Analysis (BIA) based on the recent household survey (2004)[3] suggests that the public health facilities are utilised far more by the poor than the richer groups, while the economically affluent sections of society prefer private health facilities to the public facilities (Figures 1.6 and 1.7). The richer groups prefer private facilities due to the perception that the quality of care is relatively higher and that there are no waiting times. This trend is more pronounced with respect to outpatient visits, where public facilities are utilised far less by the richer groups as compared to hospital care.

Figure 1.6

Decile Shares of Hospital Care in Public and Private Health Facilities, 2004



Source: NSS 60th Round.

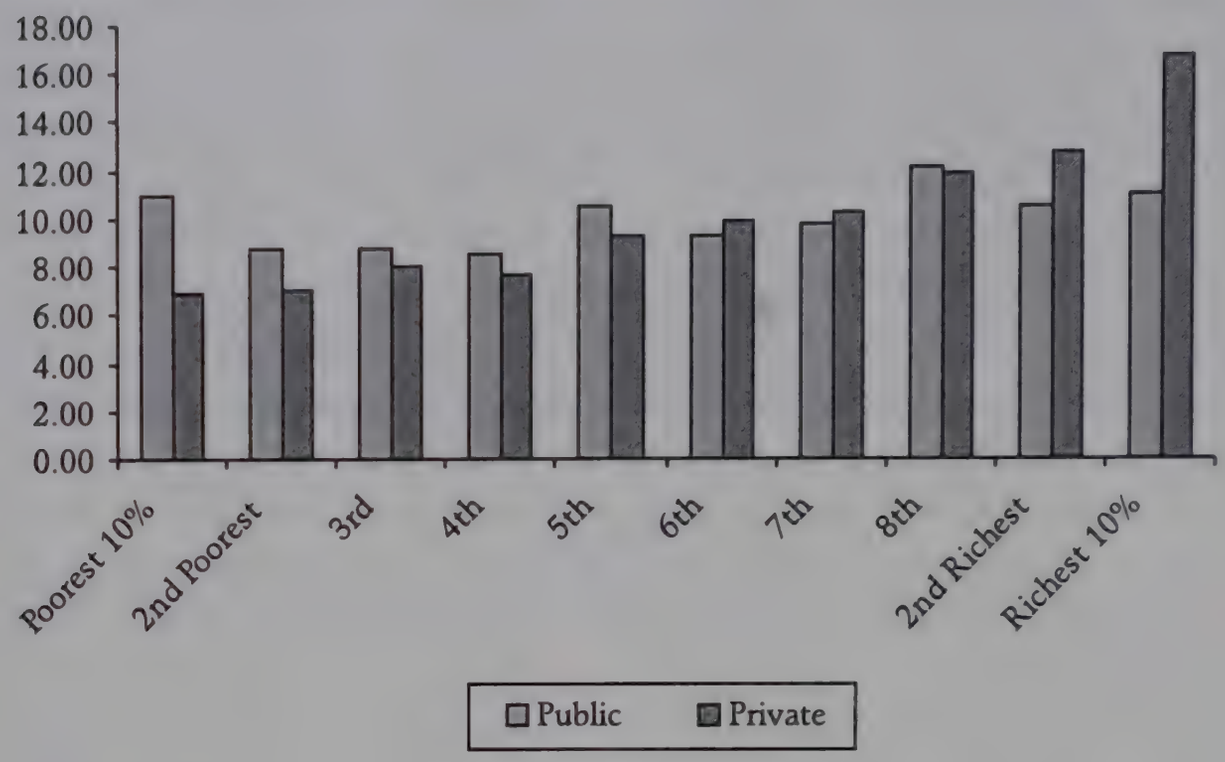
Trends and Patterns in Health System Indicators

One of the critical areas of concern in the current health system is the lack of adequate human resources at all levels of care. The challenge relates to uneven distribution of doctors, specialists and nurses and the growing threat of overseas migration along with internal migration of doctors and specialists from the public to

3. The Household Survey was conducted by the National Sample Survey Organisation (NSSO), under the name "Morbidity and Health Care", National Sample Survey, 60th Round of NSS.

Figure 1.7

Decile Shares of Outpatient Care in Public and Private Health Facilities, 2004



Source: NSS 60th Round.

private health care system. The current health workforce crisis is amply demonstrated by the poor density of health workers. According to the World Health Organization,[4] the density of doctors in India is 6 for a population of 10,000 and that of nurses and midwives is 13 per 10,000 population. This approximately works out to 19 health workers for a population of 10,000 which is far below the global average.

A cross-country comparison of health worker density clearly puts India way behind other countries. For instance, India currently has a doctor-population ratio of 0.6 per 1,000 persons, in comparison to 0.3 in Thailand, 0.4 in Sri Lanka, 1.6 in China, 5.4 in the United Kingdom, 5.5 in the United States and 5.9 in Cuba. As far as the ratio of nurses and midwives is concerned, India's present figure of 2.14 nurses and midwives per doctor is much lower than Sri Lanka's 3.94 and Thailand's 5.07. The shortfalls have led to a situation where the distribution of health workers has become extremely

4. *World Health Statistics, 2011.*

skewed. It is estimated that nearly three-fourths of doctors are in urban India and the rest in rural India.

Due to sustained neglect of the public health system in the past, India's health infrastructure has been inadequate and in poor condition as a result of poor upkeep. Currently, against the global average of 2.9 hospital beds, India's average is about 0.9 hospital beds per 1,000 population. In absolute terms, India has around 1.37 million hospital beds, with private sector beds (833,000) outnumbering government hospital beds (540,000). Interestingly, only about half of all government beds are functional, while the share of functional beds in the private sector is about 70 per cent.

In addition, India's government health surveillance systems are inadequate in measuring and monitoring disease prevalence and emergence of new communicable diseases, and developing models for health outcomes in the country. The key challenge is that while the surveillance in the public health system is weak, there is a complete absence of collection of vital disease prevalence data from the dominant private sector. Given poor oversight and accountability, poor implementation of existing legislation is responsible for the complete absence of surveillance of disease conditions in the private sector. Due to poor infrastructure in the public health system and absence of the private sector in rural areas, referral linkages and follow-up services are very weak, rendering the connectivity between primary, secondary and tertiary services dysfunctional. This has led to a scenario where government tertiary care hospitals in urban areas tend to be overcrowded and ineffective in the delivery of health care.

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2

SAKTHIVEL SELVARAJ, ANUP KARAN,
MAULIK CHOKSHI, HABIB HASAN FAROOQUI
and PREETI KUMAR

Economic Barriers to Access to Medicines in India

Underfunded Public Health System

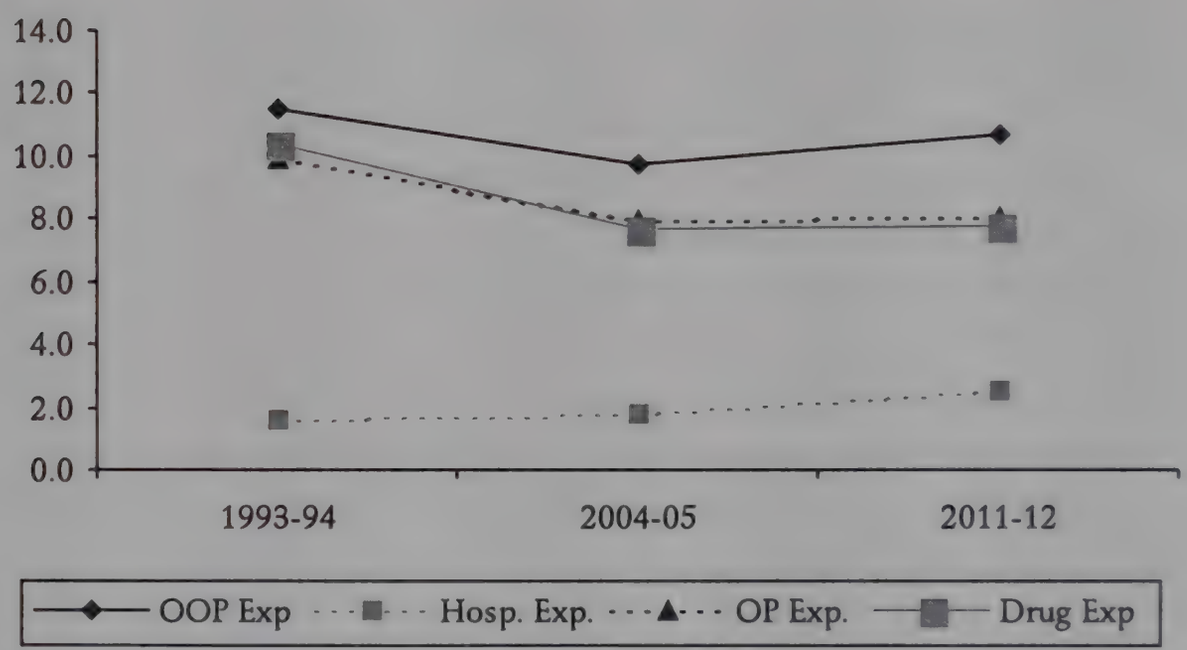
India's perennially and grossly under-resourced public health system is responsible for the ills that afflict the health sector, with poor health outcomes and inadequate financial risk protection. Governmental neglect of the health system since the initiation of economic reforms in the early 1990s has exacerbated the situation, leaving health care financing and delivery largely in the private domain. India currently spends around 4.2 per cent of its GDP on health care, of which the share of public expenditure is a little over one-fourth, the remaining 70 per cent being accounted for by household out-of-pocket (OOP) expenditure (Government of India, 2009). The share of public financing is far below that of most comparable developing countries and, even more so, the industrialised countries. A prepayment and risk-pooling mechanism, which is critical in ensuring financial risk protection, is almost absent in the country.

While most industrialised countries and a host of other low- and middle-income countries increasingly rely on either tax-based financing or social health insurance in financing health care, India does not have a robust tax-based health financing system, nor, until recently, could it rely on the social health insurance system. Since 2007 there has been a significant change in the latter scenario due to a plethora of publicly financed health insurance schemes,

introduced by both the central and state governments, including the former's Rashtriya Swasthya Bima Yojana (RSBY), the Rajiv Aarogyasri in Andhra Pradesh, the Tamil Nadu Chief Minister's Health Insurance, and Vajpayee Aarogyasri in Karnataka. There has been a dramatic increase in health coverage from less than 50 million persons in 2007 to almost 300 million in 2011. The major thrust of these programmes, however, has been on hospitalisation coverage, especially the surgical component of inpatient care. This is in direct conflict with expenditure evidence, which points to outpatient care, especially the drugs component, as accounting for over 70 per cent of all household expenditure on health care.

Figure 2.1

Trends in Share of OOP Spending in India from 1993-94 to 2011-12
(As Percentage of Households' Non-Food Expenditure)



Source: Estimated from Unit Level Records of respective Consumer Expenditure Rounds, National Sample Survey Office.

The figures, however, hide diverse spending patterns among states, with wide disparities in public and private expenditure. Household expenditure on medicines has been estimated to account for over 80 per cent of the health care expenditure in economically poor states such as Bihar and Uttar Pradesh, while in states such as Tamil Nadu and Kerala, with larger investments by the public sector, it is about two-thirds of the total household expenditure.

Significantly, the latter are the states whose health status and health system indicators are relatively robust. Households' OOP payment has been growing quite substantially in the past two decades and now accounts for around 11 per cent of non-food expenditure (Figure 2.1). Over two-thirds of that spend is on outpatient expenditure while the rest is accounted for by hospitalisation. Although there seems to be a marginal fall in the outpatient care expenditure of households in the last five years, hospitalisation expenditure appears to have increased in the same period.

Interestingly, the share of household OOP expenditure on health care appears to have declined marginally for the first time in decades, and in 2009-10 the decline is solely due to a fall in the share of outpatient expenditure. Hospitalisation, as a share of overall household expenditure, actually increased during 2009-10 to 3.9 per cent from approximately 3.5 per cent in 1999-2000.

Table 2.1

Share of Households' OOP Expenditure by Quintile Groups, 2009-10

Sector	*Poorest*	*2nd Poorest*	*Middle*	*2nd Richest*	*Richest*	*All*
OOP Exp.	3.74	4.57	5.11	5.84	7.23	5.73
Hosp. Exp.	26.41	30.69	32.25	34.35	33.81	32.74
OP Exp.	73.59	69.31	67.75	65.65	66.19	67.26
Drug Exp.	75.42	72.34	70.11	66.81	65.90	68.28

Source: Extracted from Unit Level Records of 66th Consumer Expenditure Round, National Sample Survey Office

Table 2.1 demonstrates the predominance of outpatient care spending of households, especially on drugs, which account for about 68 per cent of all household health care spending. While the poorest segment of the population is relatively less affected than the rich in the case of hospitalisation expenses, the burden of outpatient expenditure, more specifically drug expenditure, affects the poorest segment more than the richest quintile (see Figure 2.2).

Given the presence of substantial financial and physical barriers, poor households either forego treatment or are forced to seek expensive health care, thus spending a significant amount of their resources. As a consequence of recourse to expensive health care,

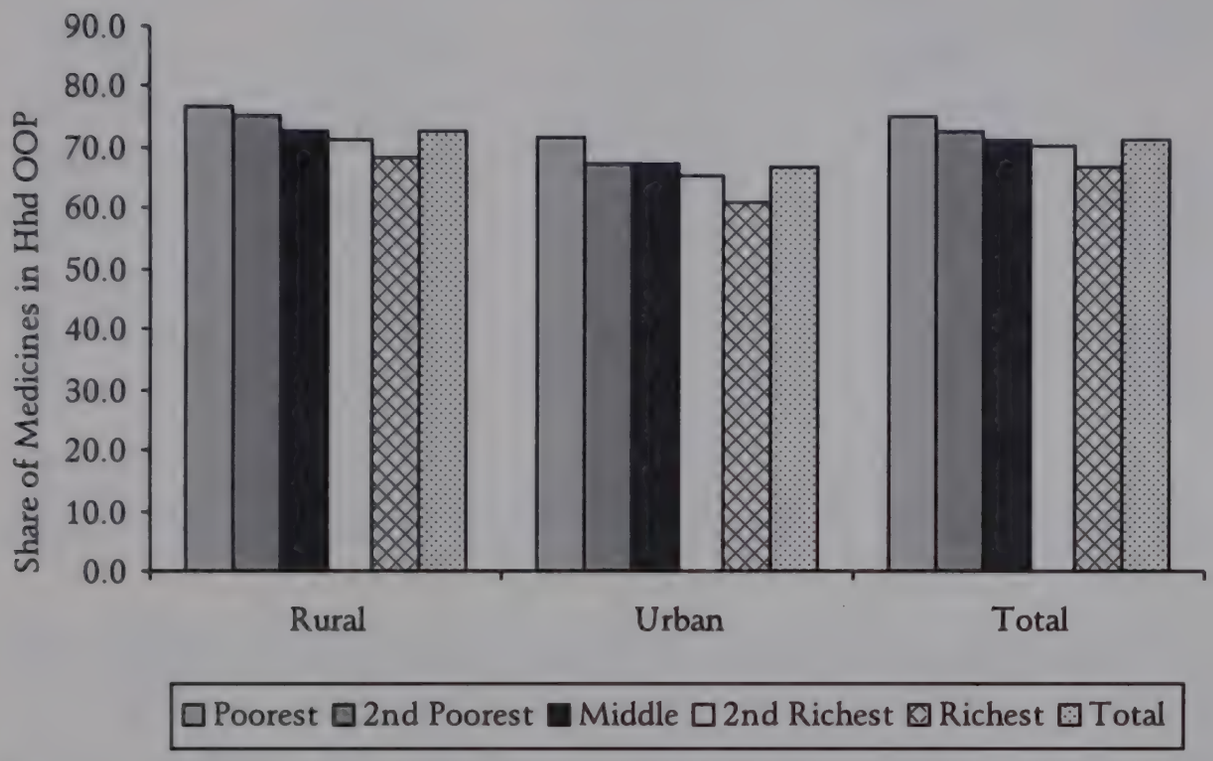
they become vulnerable to catastrophic spending, which leads them into impoverishment. This has assumed a serious dimension in recent years, and it is estimated that nearly 39 million people were pushed below the poverty line in 2004-05 because of paying out-of-pocket, over and above those already poor (Selvaraj and Karan, 2009; 2012).

An analysis of household expenditure by quintile groups reveals that OOP expenditure is progressive as only 3.74 per cent of the poorest households' spending goes into health care, as against 7.23 per cent for the richest quintile group. Inequity in the household spending pattern is comparatively higher in rural than urban India. This could be attributed to better physical access to health care facilities in urban areas and, to a lesser extent, to the relatively better purchasing power of the poor in urban areas. This is clearly the case for hospitalisation expenses, where the difference between the rich and the poor is substantial in rural areas and less so in urban areas.

Table 2.1 also shows the proportionate share of hospitalisation expenditure as against outpatient expenses. Currently, hospitalisation expenses account for only about one-third of the overall OOP expenditure while the remaining two-thirds are accounted for by outpatient care expenditure, especially on drugs. It should be noted that the current focus of publicly financed health insurance schemes is directed towards hospitalisation episodes to the neglect of outpatient care. Further, it is seen that a relatively larger proportion of poor and other economically vulnerable sections (second poorest quintile and middle class) attribute the burden of health spending to outpatient care. This is especially true of drug spending, where medicines account for three-fourths of all OOP spending of the poor while for the rich, it accounts for just under two-thirds. The current thrust of insurance schemes clearly demonstrates the distortion and lopsided priorities of the programmes, priorities that are in direct conflict with the evidence.

Figure 2.2

Share of Medicines in Households' OOP Expenditure by Quintile Groups, 2011-12



Source: Authors' calculation from unit level records of National Sample Survey, 2011-12, National Sample Survey Organisation, New Delhi.

While it is important to understand the trends and patterns in OOP spending of households, it is also worth probing the impact of OOP expenditure on catastrophic spending and impoverishment status. When households incur health care expenditure in excess of 10 per cent of their overall spending, they are deemed to be incurring catastrophic payments. The incidence of catastrophic expenditure is typically measured by the headcount of households who exceed the minimum threshold of OOP spending. At the 10 per cent threshold level, 7.4 per cent of the poorest households in India were reported to have incurred catastrophic spending during 2004-05 (Table 2.2). There has been a marginal rise in the number of poor households incurring catastrophic payments in 2009-10 compared to 2004-05. However, there has been a decline in the incidence of catastrophic expenditure among the better-off economic groups. In the case of inpatient expenditure, catastrophic incidence has gone up in every quintile.

Table 2.2

Percentage of Households Facing Catastrophic Expenditure on Health in 2004-05 and 2009-10

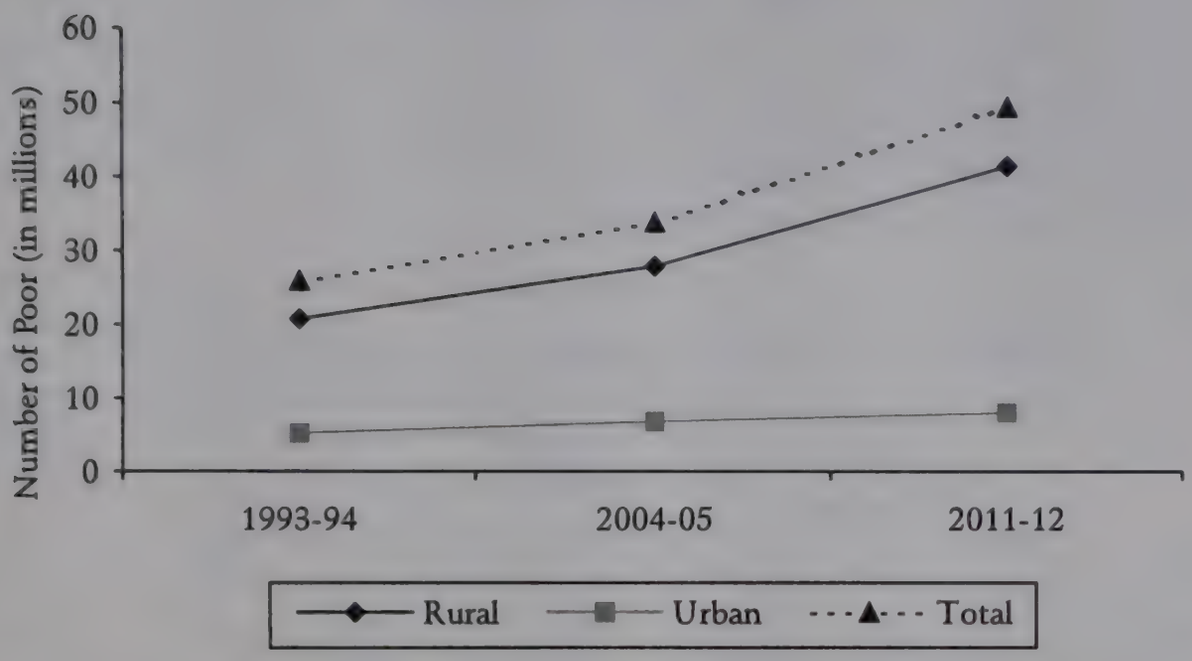
Quintile Groups	*OOP Expenditure*		*Inpatient Expenditure*		*Outpatient Expenditure*		*Drugs Expenditure*	
	2004-05	*2009-10*	*2004-05*	*2009-10*	*2004-05*	*2009-10*	*2004-05*	*2009-10*
Poorest	7.425	7.656	0.772	1.082	6.853	6.329	5.440	4.523
2nd Poorest	10.967	9.875	1.791	1.980	9.523	7.394	7.622	6.012
Middle	12.886	12.237	2.466	2.770	10.874	8.848	8.878	7.392
2nd Richest	17.882	16.197	3.507	4.496	15.109	10.979	12.593	9.591
Richest	23.690	22.456	7.318	7.954	18.293	16.207	16.713	14.852
All	14.570	13.684	3.171	3.656	12.130	9.951	10.249	8.474

Source: Extracted from Unit Level Records of 66th Consumer Expenditure Round, National Sample Survey Office

Turning to the impoverishment impact of households' OOP spending, there is clear evidence that OOP payments not only push a large number of households below the poverty line, but also plunge into deeper poverty those already under the poverty line. In India the latest estimate of the population living below the poverty line is 27.50 per cent for 2005-06 (28.30% in rural and 25.70% in urban areas). If we discount the health expenditure (OOP) of the households from their overall consumption expenditure, the headcount of poverty rises to 31.20 per cent in 2004-05. In 2004-05 the difference in the poverty levels due to OOP health expenditure was as high as 3.6 per cent (Selvaraj and Karan, 2009). In terms of absolute headcount, this means an additional 39 million people dragged below the poverty line due to OOP payments. The poverty impact of OOP spending has been rising in terms of proportion as well as absolute numbers. The additional share of the population pulled below the poverty line has increased from less than 3 per cent in 1993-94 to some 3.6 per cent in 2004-05. Thus, the absolute number of those dragged into poverty escalated from roughly 26 million in 1993-94 to nearly 39 million in 2004-05 (Figure 2.3).

Figure 2.3

Increase in Poverty due to OOP Payments



Source: Authors' calculation from Unit Level Records of respective Consumer Expenditure Rounds of the National Sample Survey, National Sample Survey Organisation, New Delhi.

The rise in the additional number of poor because of OOP payments reflects the impact of such payments on households. Although over the years the overall poverty ratio has been declining, the impact of OOP expenditure on poverty has witnessed a rise. Moreover, it is critical to observe that despite lower per capita OOP spending in rural areas compared to urban India, the impact of OOP spending in terms of the poverty headcount was higher in rural areas in 2004-05. This indicates the increasing impoverishment impact of OOP expenditure in rural areas.

While underinvestment in health care services is a key reason for poor health outcomes and distorted health sector development, one of the critical reasons for poor financial risk protection is over-reliance on OOP spending, especially for drugs. This is a direct result of gross underfunding of medicine procurement by the government. The government (both central and state) allocates only some 13 per cent of its health funding to the procurement of drugs, supplies and consumables (Table 2.3).

This situation is compounded by an abysmally deficient coverage of drug spend by social health insurance where reimbursement

for drugs is hardly part of any benefit package. Other than the Employees' State Insurance Scheme (ESIS) and Central Government Health Scheme (CGHS), no other scheme, whether private or public, such as the central-government-funded RSBY or the state-government-sponsored Rajiv Aarogyasri Health Insurance in Andhra Pradesh or Kalaignar's Health Insurance Scheme in Tamil Nadu, provides for drug reimbursement.

Table 2.3

State-wise Government Spending on Health Care and Drugs

State	*Overall (2001-02) (₹ '00,000)*	*Per Capita (₹)*	*Drug Exp. as % of HE*	*Overall 2010-11 (₹ '00,000)*	*Per Capita (₹)*	*Drug Exp. as % of HE*
Assam	1,530	5.7	4.7	8,635	28.5	5
Bihar	2,203	2.6	3.1	13,350	13.8	7
Gujarat	2,693	5.3	3.7	15,431	26.4	7.6
Haryana	3,096	14.7	9.8	6,090	24.2	5.5
Kerala	12,420	38.9	17	24,861	72.3	12.5
Maharashtra	20,305	20.8	11.3	20,882	18.7	5.2
Madhya Pradesh	7,921	13.0	11.8	12,213	17.1	9.3
Punjab	916	3.7	1.4	1,545	5.6	1
Rajasthan	9,045	15.9	9.3	3,854	5.7	1.5
Uttar Pradesh	7,104	4.2	5.2	31,481	15.9	5.3
Jharkhand	NA	NA	NA	2,716	8.7	3.4
West Bengal	5,798	7.2	4.3	21,403	24.1	6.8
Andhra Pradesh	12,704	16.6	9.6	23,458	27.9	10
Karnataka	7,783	14.7	7.9	14,831	25.1	6.3
Tamil Nadu	18,097	28.9	15.3	43,657	65.0	12.2
Himachal Pradesh	NA	NA	NA	1,122	16.6	1.9
Jammu and Kashmir	NA	NA	NA	4,550	39.2	4.3
Central Government	72,649	7	12.2	253,368	21	15
All India	188,903	18	9.6	503,447	43	13

Notes: Many states report drug expenditure under the category of material & supply.

Material & supply includes hospital accessories, bedding cloth, material supply, laboratory charges, X-ray materials and others, and here we have included material & supply only.

Only the figures for 17 states are reported in the table, accounting for around 87 per cent of the overall Indian population.

Estimates for 2010-11 are budget estimates.

HE refers to health expenditure of the state/central government.

Source: Budget document, respective state governments and central government

While inadequate funding is certainly a vital element, inefficient use of available resources for drugs is an equally alarming trend. The distorted priorities of public spending on drugs are clearly visible from Table 2.4. In terms of level of care, *viz.*, primary, secondary and tertiary care, there is a clear trend where several states in India appear to direct a considerable share of drug expenditure towards tertiary care. Rajasthan and Odisha have over 90 per cent of resources going towards drug expenditure in tertiary care, followed by Gujarat, West Bengal and Punjab, which have allocated over 70 per cent of drug expenditure to tertiary care.

Table 2.4

Sectoral Allocation of Government Drug Spending, 2008-09

State	*Overall Drug Expenditure*	*Drug Exp. on Tertiary Care*	*Drug Exp. on Primary and Secondary Care*	*Drug Exp. on Urban Services*	*Drug Exp. on Rural Services*
	(₹ Million)	*(As Percentage of Total Drug Expenditure)*			
West Bengal	1,364	73.08	26.92	74.2	25.8
Odisha	153.7	95.41	4.59	95.82	4.18
Uttar Pradesh	2,079.8	54.5	45.5	55.25	44.75
Madhya Pradesh	646.3	62.71	37.29	68.28	31.72
Gujarat	479.1	84.17	15.83	94.91	5.09
Chhattisgarh	206.3	24.34	75.66	87.35	12.65
Tamil Nadu	1,493	40.04	59.96	45.23	54.77
Bihar	664.4	56.86	43.14	57.25	42.75
Karnataka	1,204.3	46.07	53.93	46.68	53.32
Jharkhand	151.5	43.56	56.44	44.16	55.84
Rajasthan	1,066.3	96.4	3.6	96.66	3.34
Punjab	110.1	71.25	28.75	77.84	22.16
Kerala	1,214.9	66.51	33.49	72.49	27.51

Source: Respective budget documents of states, 2008-09

On the other hand, in Chhattisgarh, Tamil Nadu, Jharkhand and Karnataka, over half of all drug spending goes into primary and secondary care. Chhattisgarh is an outlier from the other states, as three-fourths of all its drug spending went into primary

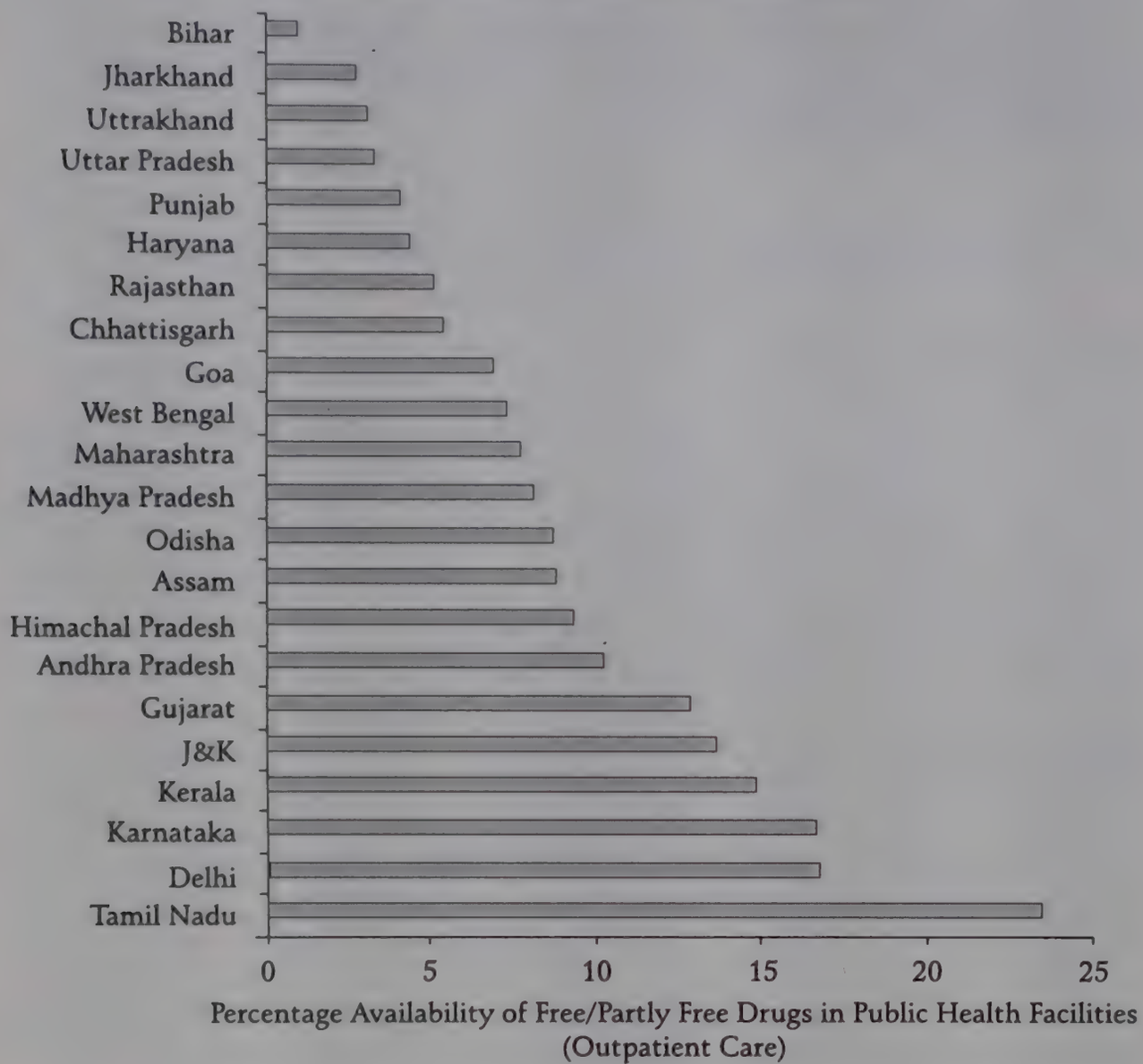
and secondary care, and tertiary care accounted for just one-fourth of the expenditure. It is also interesting to note that Bihar's drug spending pattern is not significantly skewed, unlike other less developed states. The allocation of funds towards primary, secondary or tertiary care also reflects the rural-*versus*-urban fund split. To be specific, since tertiary care is reflective of urban care services, higher or lower drug spending in tertiary care mirrors drug expenditure in urban *versus* rural areas.

Higher budget allocations *per se* may not suffice in the face of a system plagued by weak institutions and poor governance. For instance, money allocated for certain services such as drug procurement and distribution may not reach either the frontline service providers or the intended beneficiaries. Therefore, without a concomitant reliable and efficient supply chain management system extending from manufacturer to patient, the allotted funds may not reach the intended beneficiaries. This would result in acute shortages and chronic stock-out of drugs.

Figure 2.4 reveals the predominance of private chemists and the poor record of public health facilities in distributing free medicines. It also shows the availability of free or partially free drugs in outpatient care. It is apparent that southern states, in particular, appear to have relatively better access to medicines compared to other states, including those which are relatively better off economically. The time-tested model of the Tamil Nadu Medical Services Corporation (TNMSC) and its success is clearly reflected in the share of people able to obtain free/partly free medicines from public health facilities. The National Sample Survey (NSS) shows that in Tamil Nadu availability of drugs from public health services is around 25 per cent, followed by Karnataka, Kerala and Delhi. The lower percentage share in other states (including economically well-off states such as Maharashtra, Punjab, Haryana etc.) indicates a higher reliance on private chemists. Although the evidence dates back to 2004, much of the story remains true even today. But it can be conjectured that the relative share of free medicines available in public health facilities must have improved after the National Rural Health Mission (NRHM) was launched in 2005.

Figure 2.4

Percentage Availability of Free/Partly Free Drugs in Public Health Facilities (Outpatient Care) by State in India, 2004



Source: Extracted from Unit Level Records of National Sample Survey (Morbidity and Health Care Utilisation), 2004

Table 2.5 shows the district-wise availability of essential drugs, stock-outs of essential drugs and average duration of stock-outs (six months prior to the survey[1]) in Tamil Nadu and Bihar, two diverse settings with different financial allocations and two different procurement and distribution systems.

As evident from Table 2.5, there is an unmistakable pattern of drug availability and stock-outs in the various facilities across the states under study. The mean availability of the basket of drugs

1. An independent survey of public health facilities in Bihar and Tamil Nadu by Public Health Foundation of India. Citation: Selvaraj *et al.* (2012).

for Bihar on the day of the survey was about 43 per cent as against roughly 88 per cent, or double, for Tamil Nadu. As far as the stock-out position was concerned, Bihar's health facilities registered an average of about 41 per cent stock-outs of drugs. On the other hand, the proportion of stock-out for Tamil Nadu was less than half that, at around 16 per cent.

Table 2.5

Availability and Stock-outs of Essential Drugs in the Districts of Bihar and Tamil Nadu

Bihar				*Tamil Nadu*			
District	*% EDL Drugs Available (Survey Day)*	*% of EDL Stock-out (6 Month)*	*Avg. Duration of Stock-out (Days)*	*District*	*% EDL Drugs Available (Survey Day)*	*% of EDL Stock-out (6 Month)*	*Avg. Duration of Stock-out (Days)*
Begusarai	52.27	38.63	114.08	Coimbatore	90.91	13.64	25
Darbhanga	0	100.0	180	Cuddulore	81.81	21.21	44.52
East Champaran	31.82	54.54	126.2	Trivillur	81.82	18.18	49.17
Gopalgunj	45.45	38.63	87.7	Erode	90.9	18.18	60.56
Jhanabad	38.63	47.72	82.2	Kanyakumari	90.9	6.818	6.67
Lakhesarai	59.09	31.82	87.86	Nagapattinam	77.27	18.18	103.75
Madhubani	40.9	34.09	78.7	Namakkal	100	9.09	40.0
Muzaffarpur	27.27	100.0	180.0	Nilgiri	86.36	13.64	73.33
Nalanda	45.45	22.73	102.0	Perambur	90.91	18.18	75.0
Patna	25.75	43.9	74.9	Salem	86.36	13.64	35.0
Purunea	60.60	45.45	70.3	Shivganga	90.91	27.27	30.17
Samasthipur	36.36	36.36	91.25	Tanjavore	95.45	29.54	48.25
Saran	50.0	33.33	87.5	Thiruvnamalllai	81.82	13.64	75.0
Siwan	61.36	27.27	131.85	Tirunellveli	81.81	12.12	56.25
Vaishali	63.64	31.82	58.57	Tuticorin	77.27	27.27	72.0
Bhojpur	31.8	18.18	121.2	Villupuram	90.9	22.72	41.25
Katihar	36.36	31.82	111.43	Virudnagar	90.9	2.27	25.0
				Vellore	93.18	9.09	42.5
Overall for state	**42.64**	**41.35**	**105.0**	**Total**	**87.76**	**16.37**	**50.19**

Note: EDL: Essential Drug List.

Source: Selvaraj *et al.* (2012).

Within the states, there are wide variations between districts, especially in Bihar. The availability of drugs in the drug basket ranged from 0.0 per cent for Darbhanga district to 63.64 per cent for Vaishali. The proportion of stock-out ranged from 100 per cent in Darbhanga and Muzaffarpur to 23 per cent in Nalanda. In contrast, in Tamil Nadu, drug availability ranged from as high as 100 per cent in Namakkal to the lowest recorded at 77 per cent in Nagapattinam and Tuticorin, far above the average for Bihar. In contrast to Bihar, in Tamil Nadu the proportion of stock-outs was below 30 per cent for all the districts.

For Bihar as a whole the average stock-out duration was 105 days, with the durations in individual districts ranging from a low of 58 days in Vaishali to a high of 180 days for Darbhanga and Muzaffarpur. Districts with a 100 per cent stock-out obviously had no drugs available from the basket of EDL. However, we found that drugs from the same therapeutic categories were available in health facilities on prescription for beneficiaries, but these were not included in our analysis as the common denominator for study was the EDL-based basket of medicines. In Tamil Nadu the average duration of stock-out was 50 days, with a deviation ranging from 103 days in Nagapattinam to 7 days in Kanyakumari. The duration of drug stock-out in Tamil Nadu was less than half of that in Bihar.

Unreliable and Inefficient Medicine Supply Systems

One of the key components underlying access to medicines is a reliable supply chain management system that includes the procurement and distribution logistics of drugs and vaccines. An efficient procurement supply chain management system is predicated upon the principle of transparency in the process of selection of drugs, quantification of drugs, procurement process (including tendering process, bid opening process, award conditions, payment mechanism) and quality control procedures. Inefficiency in any one of these areas can lead to sub-optimal performance of the system, resulting in frequent stock-outs and acute shortages of essential drugs. In addition, poor procurement practices may lead to a non-competitive environment with fewer choices of suppliers and higher prices of drugs for the health system.

There are different procurement and supply chain management systems that are followed in India. For the centrally supported programmes, multiple agencies assist the Ministry of Health in the procurement process. States follow various types of procurement mechanisms: pooled procurement at the central level, centralised procurement and decentralised distribution in Tamil Nadu, decentralised procurement in Chhattisgarh and the "cash and carry" model in Bihar.

The procurement process followed in several states is not based on standard operating procedures. There is no clear documentation of the entire procurement process that needs to be followed. Lack of clarity results in a multitude of interpretations and also limits confidence generation amongst the suppliers. There is also a top-down approach rather than a need-based approach for drug supply. In addition, the lack of dedicated warehouses and a weak supply chain system have a serious effect on storage and delivery of drugs. All these limitations are expected to adversely affect competition, price, quality and timely availability of drugs to the frontline health care providers.

Interestingly, the tender document process in Tamil Nadu has significantly strengthened the procurement process by establishing clear guidelines on the quantity and quality of the products, award of contracts, payment mechanisms, quality assurance protocol and dispute settlement procedures. Drug procurement itself is a transparent and inclusive process in the state, based on its Tamil Nadu Transparency in Tenders Act, 1998 and Tamil Nadu Transparency in Tenders Rules, 2000. The procurement cycle is based on the Transparency Act and Rules while its standard bidding documents guide procurement of drugs and medicines and medical equipment.

To increase the system's responsiveness, a certain share of the dedicated procurement budget always rests with the facility to respond to emergency requirements. The TNMSC also allows for a maximum 15 per cent price rise from the previous year's rates for the manufacturers. The corporation also follows a "two-bid system", one for technical specification and the other for financial particulars of the manufacturers. The process of awarding the rate contract,

where the commercial bids are opened in front of all successful technical bidders, has also enhanced transparency and confidence in the procurement system. Thus, a centralised procurement and decentralised drug distribution system appears to be the key to improve and sustain good governance in the medicine supply system.

Forecasting and procurement planning is critical to the entire procurement cycle. Currently, several states in India do not have a forecasting or planning mechanism required for the initiation of the procurement cycle. For instance, in Bihar, available evidence shows that in a period of three years spanning 2005-2008, the list of drugs that were procured were not on the EDL list nor on the rate contract, and varied considerably. As seen in Table 2.6, the number of drugs procured in 2007-08 was 369, compared to 91 and 89 in the previous two years.

In 2007-08, Bihar assisted by a technical support agency, started implementing procurement sector reforms as a part of health sector reforms. The number of companies submitting successful tenders and the number of products selected have seen an increase over a period of time. However, there are a considerable number of drugs which continue to be procured without any bid or are not procured by the State Health Societies (SHS). The Bihar SHS compare the rates of the bidders with other states like Kerala, Rajasthan and the Employees State Insurance Corporation before finalising the contract. In the case of a single bidder, a reference pricing mechanism based on prices of drugs in two to three neighbouring states is used for procurement.

Table 2.6

Competitive Bidding Process in Drug Procurement in Bihar

	2005-06	*2006-07*	*2007-08*
Number of drugs to be procured	89	91	369
Number of firms submitting bids	29	25	31
Number of successful technical bids	14	19	27
Number of successful financial bids	9	13	22
Number of products selected	50	54	141
Number of drugs with no bidder	39	37	No Record

Source: Documents obtained from state

The TNMSC floats tenders for an EDL of 262 drugs annually and has been successful in getting bids for most of the EDL. Further, it has managed to stimulate considerable competition amongst drug manufacturers; interest in the state drug procurement model is evident from Table 2.7. Around 100 companies showed interest in supplying drugs to the state through the TNMSC in 2007-08. The tender document also stipulates the condition that in the case of unused drugs, the supplier will be asked to take back the surplus stock. The rate contract is done each year and is valid for a year or until further communication by the TNMSC. As part of procurement planning, the requirement of drugs for the current year is based on the previous year's consumption of drugs.

Table 2.7

Number of Companies Applying for Tender in Tamil Nadu

	2005-06	*2006-07*	*2007-08*
Total number of drugs procured	270	271	252
Total applicants accepted	76	77	65
Total applicants rejected	59	47	35
Total applicants	135	124	100

Source: Documents obtained from state

A reliable drug distribution system is equally as important as an efficient procurement system. The TNMSC, drug warehouses and health facilities are linked through Electronic Data Processing (EDP) units. The TNMSC places purchase orders based on three months' base stock and two months' pipeline stock. Public health facilities, on the other hand, are issued "pass books" wherein the current year's value is determined based on the previous year's consumption pattern and patient load (National Health System Resource Centre, 2009). On average, the primary health centres are provided with approximately ₹ 150,000-200,000 per annum in their pass books. Often public health facilities are given additional funds during the financial year if their needs exceed the value of drugs allocated to them at the beginning of the year.

To take advantage of economies of scale and the monopsony power of the institutions (here the government), state and central governments must aim to procure drugs at a centralised level in each state and at the central level. Tamil Nadu and Kerala, for instance, procure drugs at the centralised level at rock-bottom rates closer to the manufacturer's cost. When such a model is replicated, similar results ensue. A recent initiative in Chittorgarh, a district in Rajasthan, demonstrates the monopsony power of government in buying generic drugs directly from the manufacturers. Table 2.8 provides medicine price data in three settings: the Tamil Nadu procurement price (through the TNMSC), the Chittorgarh district procurement price and the market price for therapeutically similar drugs. It is apparent that TNMSC drug prices are several times lower than market prices and also less than Chittorgarh prices across all therapeutically similar medicines. Interestingly, Chittorgarh prices include a 20 per cent mark-up for retailers plus a 4 per cent value-added tax. An efficient procurement mechanism therefore can obtain maximum value for money, by eliminating intermediaries and their margins in the supply chain.

Conclusion

There is an urgent need to scale up public spending on drugs, vaccines and other diagnostics. The current spending of governments (both state and central) must be scaled up from 0.1 per cent of GDP to at least 0.5 per cent of GDP in the next five years. This is expected to result in a significant reduction in household OOP expenditure and thereby provide the much-needed financial risk protection. It is also likely to substantially reduce the current existing inter-state and inter-district disparities.

In addition to scaling up public spending, the government procurement and distribution system must be made more efficient and reliable. This could be modelled on the TNMSC and could take the form of centralised procurement and decentralised distribution. This would mean procuring medicines based on the EDL at the centralised level in each state. Value for money can be obtained as such a model is expected to achieve economies of scale due to use of monopsony power. In order to obtain quality generic drugs for

Table 2.8

Comparison of Procurement and Market Prices for Therapeutically Similar Medicines

Market Leader Medicine	*Active Pharmaceutical Ingredient (API)*	*TNMSC Price*	*Chittorgarh Price (₹)*	*Market Price*	*Market Price Exceeds TNMSC Price (Number of Times)*
Monocef	Ceftrixone (1g; inj)	12.39	17.47	179 (Merind)	14.45
Cifran (50mg; 10 tabs)	Ciprofloxacin	9.82	6.99	98.6 (Ranbaxy)	10.04
Amarly (1mg; 10 tabs)	Glimepride	0.75	6.24	65 (Aventis)	86.67
Glycomet GP (1mg-500mg; 10 tabs)	Metformin + Glimepride	NA	9.48	66.2 (Aventis)	6.98
Omex (20mg; 10 caps)	Omeprazole	2.14	5.49	79.4 (Zydus)	37.10
Rantac (150mg; 10 tabs)	Ranitidine	1.85	3.74	18.9 (Cipla)	10.22
Aten (50mg; 14 tabs)	Atenolol	1.14	4.37	57.5 (FDC)	50.44
Storvas (10 mg; 10 tabs)	Atrovastatin	2.09	12.36	110 (Cadilla)	52.63
Methergin (0.2mg/ml; inj)	Methyl ergotamine	1.14	3.12	19.1 (Novartis)	16.75
Zentel (400mg; 10 units)	Albendazole	4.55	13.70	17 (Glaxo)	3.74

Note: Chittorgarh prices are L1 prices (ex-factory) + 20% mark-up for retailer + 4% VAT (value-added tax).

Source: A variety of data sources were used. The market leader is determined based on IMS Health, 2009 data. TNMSC prices are from tender prices as quoted in TNMSC websites. TNMSC prices are for a pack of 10x10, but for the sake of consistency, we have converted them here into a pack of 10 tablets/capsules. Market prices were obtained from *http://patientindia.com/resultDetails.php?searchC=1&brandId=510&genId=50&sta*.

the system, a two-bid transparent procurement is required across all states. In addition, each district must be equipped with at least one warehouse, so that the centralised procurement unit and the public health facilities are reliably linked and acute shortages and chronic stock-outs in the facilities are avoided.

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3

SAKTHIVEL SELVARAJ and
HABIB HASAN FAROOQUI

The Price Barrier to Access to Medicines

Current Situation

India's current ascendance to the position of "global pharmacy" for low- and middle-income countries cannot be disputed. From a position of net importer in the pre-1970s era, India is currently a net exporter of quality and cheap generic drugs across the world (Government of India, 2006). In terms of both bulk drugs (active pharmaceutical ingredients—APIs) and formulations production, India's drug manufacturing capacity and its capability to "reverse engineer" is considered to be amongst the top in the developing economies. However, due to the crumbling and depleted condition of the public health care system in India, most of the drugs are out of stock or the system simply does not have adequate resources to buy them. This has largely resulted in a private sector takeover of the health care system in the country, due to which households are increasingly paying out-of-pocket (OOP) for health care, more so for drugs (Selvaraj, 2005). Hence, a substantial proportion of the population with extremely low purchasing power is exposed to the open drug market (WHO, 2007).

Price Regulation of the Drug Market

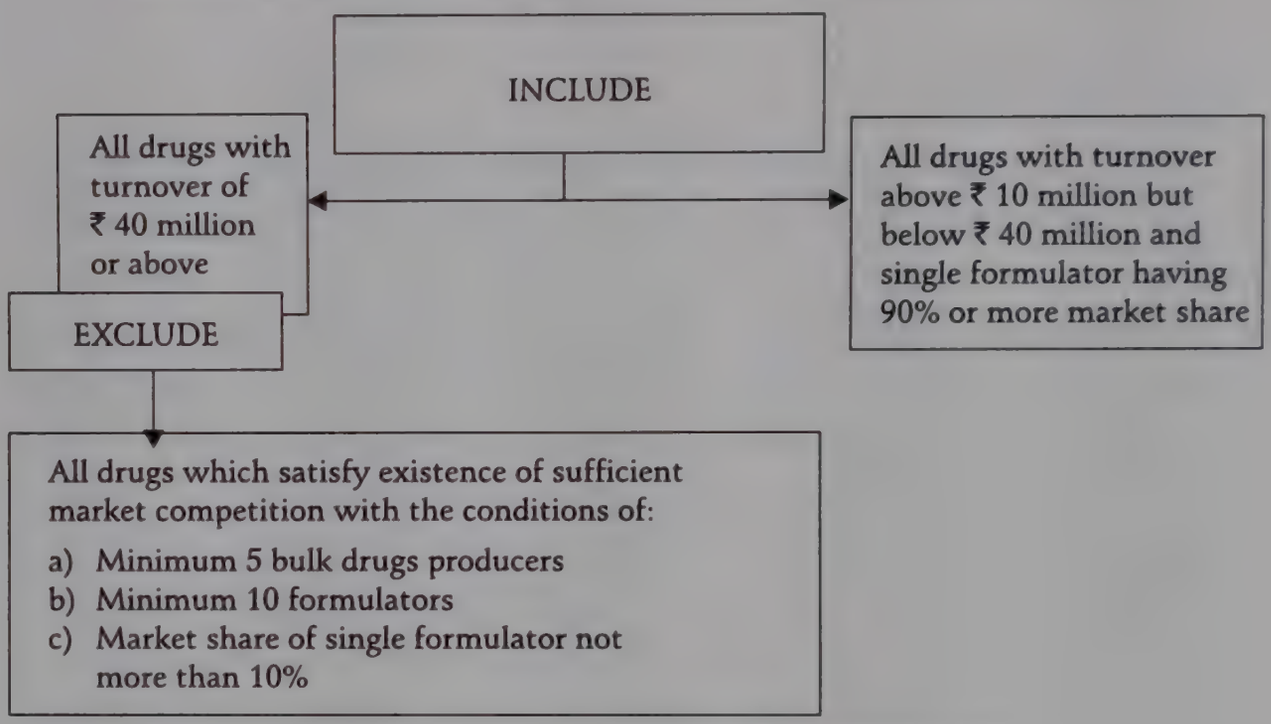
Across the globe drug prices are, in one way or another, subject to controls and regulations (Henry and Lexchin, 2002). A host of policy instruments are used on a standalone basis or in combination to rein in drug prices from reaching unreasonable levels. Such controls consist of caps on mark-ups, fixed margins to wholesalers/

pharmacists, price freezes, reference pricing, ceiling on promotional expenditure and differential value-added tax on drugs.

Prices of drugs in India were once considered to be among the highest in the world (Government of India, 1975). This situation started to reverse in the 1970s, in the wake of a series of policy measures such as drug price control, process patents for drugs, etc. (Government of India, 2005).

Figure 3.1

Criteria for Inclusion of Drugs under Price Control, DPCO 1995



Notes: a) Bulk drug turnover includes local production and import values.

b) A formulator is a manufacturer of single ingredient formulation containing the subject bulk drug.

c) Market share of single formulator of single ingredient formulation of the subject bulk drug marketed in the country (as per Operations Research Group, ORG). Market share determination is from data reported in ORG, March 1990.

Source: Government of India (1999).

Again, however, the trend is seen to dismantle price controls, and the number of bulk drugs that were under price control has been brought down gradually to a minimum. In 1979, 347 bulk drugs were under price control, which came down to 166 in 1987 and this was further reduced to 142. Drastically pruning the list of drugs under control even further, the Drug Price Control Order (DPCO) of 1995 sought to limit the control to just 76 drugs. The DPCO delineates certain benchmarks on which price control is

based. These are: (i) sales turnover, (ii) market monopoly, and (iii) market competition. In effect, formulations that are under price control are those that have: (i) annual turnover of ₹ 40 million and above with a monopoly scenario (see Figure 3.1 for detailed criteria) and (ii) annual turnover of less than ₹ 40 million but not less than ₹ 10 million with less market competition. Across the board, the price control order of 1995 fixed 100 per cent maximum allowable post-manufacturing expenses (MAPE) to all drugs.

The retail price of the formulation is calculated based on the following formula:

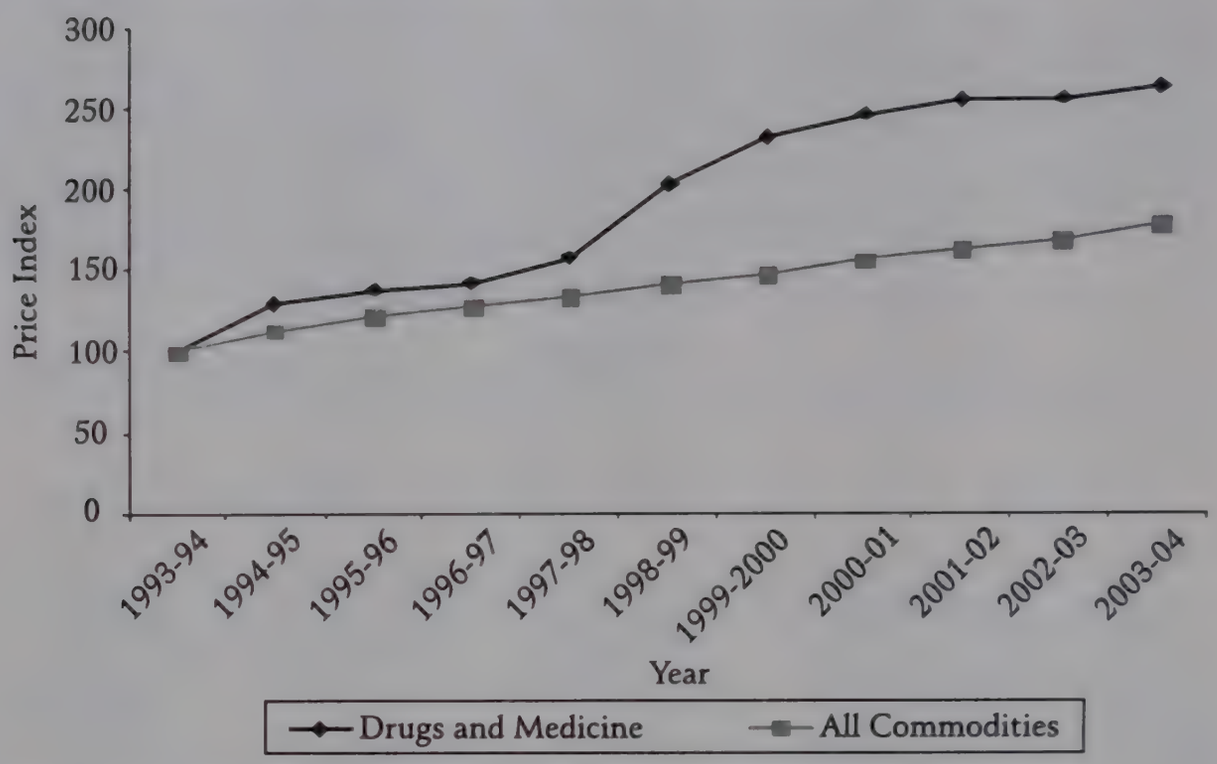
$$\text{Retail Price} = (MC + CC + PM + PC) \times (1 + MAPE/100) + ED$$

MC denotes material cost including drug cost and other pharmaceutical aids; CC indicates conversion cost; PM means packing material cost of formulation; PC connotes packing of shipment; MAPE denotes maximum allowable post-manufacturing expenses which includes trade margin; and ED indicates excise duty.

The recent policy changes have enormous implications for drug prices in India. Today only one-tenth of the drug market is price-controlled, as against nearly 90 per cent during the late 1970s. This has triggered wide debate on the rising drug prices (Rane, 1996; Srinivasan, 1999). Rane (1996), who has been consistently analysing drug prices over the years, shows that pharmaceutical price policy changes have led to a phenomenal increase in the prices of drugs of different therapeutic groups from 1980 to 1995, surpassing the general index of prices. Evidence of this can be seen in the sharply widening gap between the general price index and the pharmaceutical price index (Figure 3.2). The pharmaceutical price index provides clear evidence of a sharp and significant rise in drug prices from 1993-94 to 2003-04. There is, however, also a need to study price trends in various therapeutic segments since the overall pharmaceutical index does not capture all segments and, moreover, drugs cannot be treated as a single market but a multi-product one.

Figure 3.2

Trends in Pharmaceutical and All Commodity Price Index



Source: Reserve Bank of India.

Implications of DPCO 1995 on Drug Prices

In order to understand the underlying implications of the DPCO on prices, in this section, we analyse price trends of essential drugs that are part of DPCO 1995 and those that are outside price control, for the period spanning 1994 to 2004. The respective lists of drugs under price control and those which were decontrolled were taken from the government lists of such drugs. Further, from these lists, only essential drugs were taken. The number of essential drugs examined is as follows: (i) 31 essential drugs (out of 142 drugs under DPCO 1987) which went off price control in 1995, and (ii) 33 essential drugs (out of 76 drugs under DPCO 1995) under price control. Subsequently, the retail price of formulations involving each of these drugs was obtained from various issues of *Monthly Index of Medical Specialities* (MIMS India) spanning the decade from 1994 to 2004.

Although the initial number of products (formulations) to be considered was over 300, after elimination the number came to less than 100 products in each of the price-controlled and decontrolled

categories. Elimination of such a large number of products became imperative due to the following reasons: (i) for consistency, different dosages and strengths were ignored and only packs containing similar units, dosage forms and strengths were included; (ii) care was taken to exclude combination products as this may have yielded distorted results, although total exclusion was not possible; and (iii) products that were not listed in MIMS India continuously for 10 years were also excluded from the analysis. Depending upon the exclusion criteria outlined above, the number of formulations (products) considered varied in each therapeutic category.

Trends in Medicine Prices: Price Controlled and Uncontrolled

The price change from 1994 to 2004 is captured by working out year-on-year percentage change and cumulative 10-year price change. The annual observed trend in price change can be seen from Figure 3.3(a)-(d) for price-controlled drugs, and Figure 3.4(a)-(d) for price-decontrolled drugs. The cumulative percentage price change is provided in Tables 3.1 and 3.2.

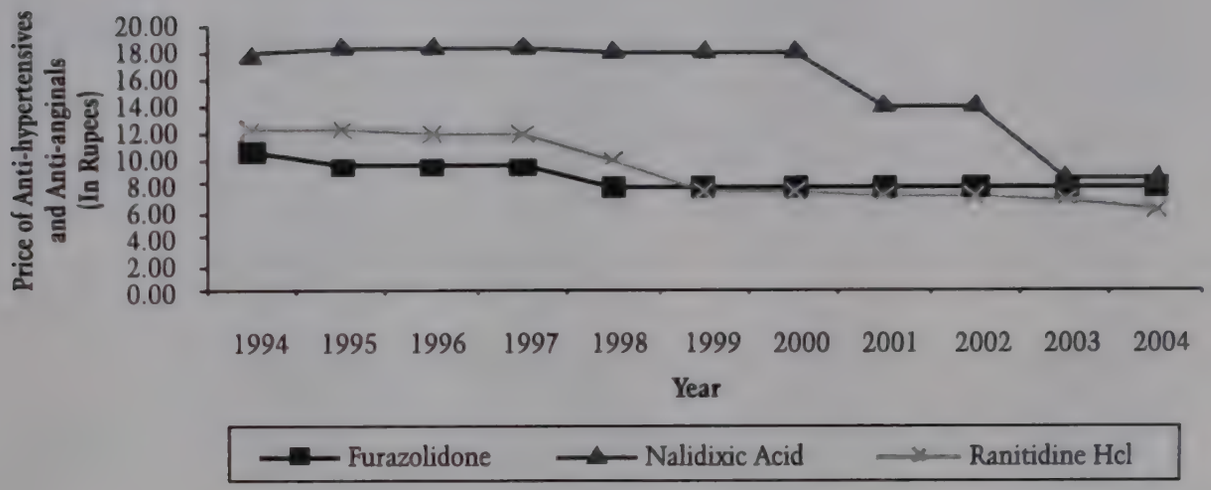
An examination of drug prices under control and decontrol throws up interesting results.

The evidence shows that drugs which are under price control have tended to either maintain a stable price or show a downward price movement. Therapeutic category-wise analysis of annual cumulative percentage price change reveals that many of the essential drugs under each therapeutic class (over half the drugs considered for the analysis) have displayed a negative price trend signifying price declines. Nalidixic acid (-7.17%), ranitidine HCl (-7.44%) and levodopa (-5.31%) are among the drugs showing substantial price decreases. Almost all antibiotic preparations which are under price control witnessed negative price growth. Other drugs whose prices registered a decline during the period under consideration include furazolindone (-2.69%), methyl dopa (-1.41%), carbamazepine (-0.11%), chlorpromazine (-0.11%), norafloxacin (-3.19%), amikacin sulphate (-0.78%), cloxacillin (-4.09%), gentamicin (-1.13%), tetracycline (-1.24%), metronidazole (-1.21%), rifampicin (-0.66%) and salbutamol (-1.60%).

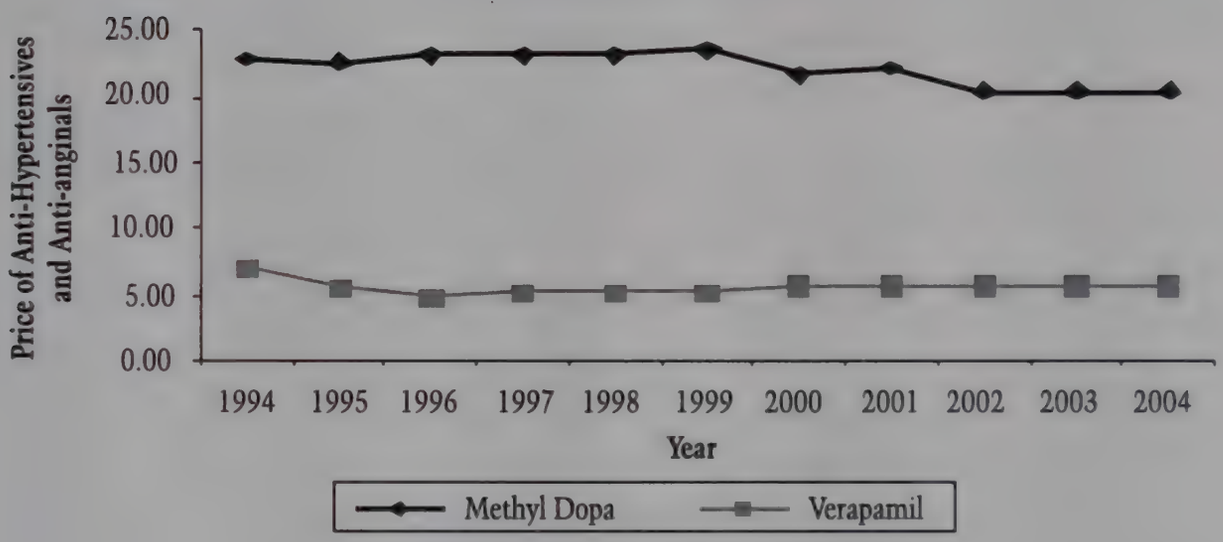
Figure 3.3(a)-(d)

Price Trends of Drugs under Control, 1994-2004

(a) Alimentary System



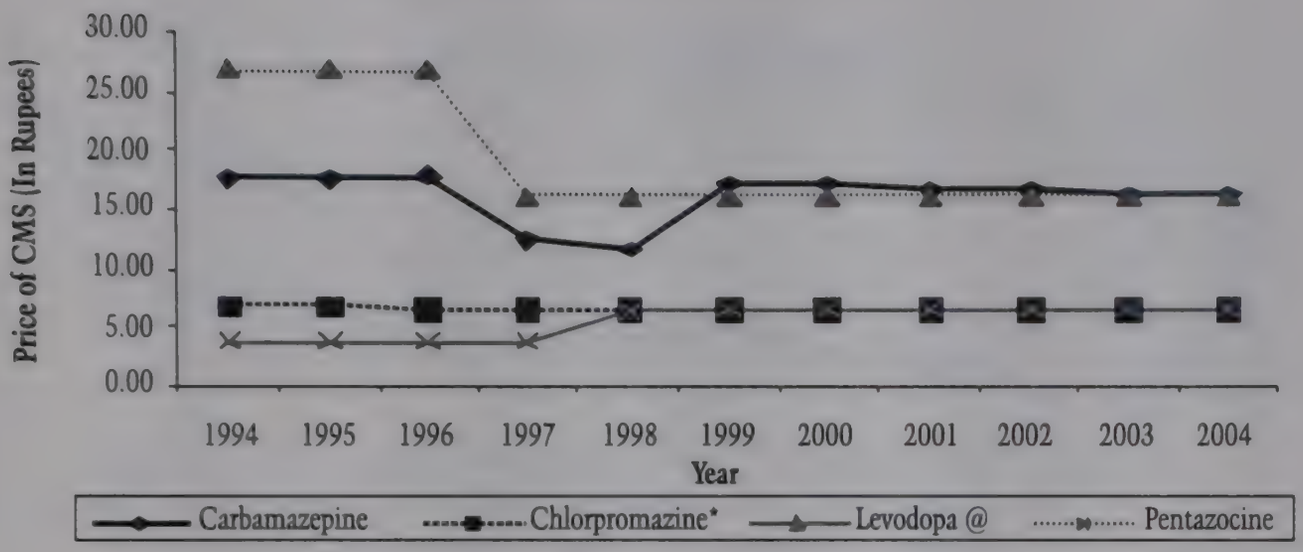
(b) Cardiovascular System



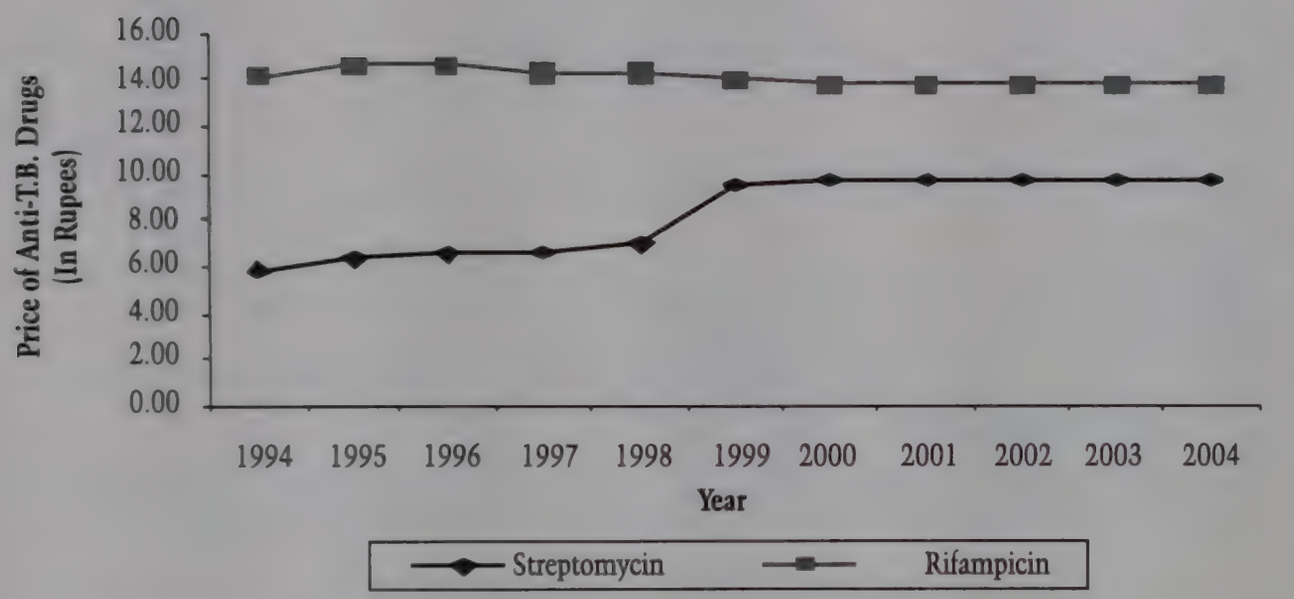
Three segments which appear to have gone against the general trend are anti-tuberculosis drugs (streptomycin), anti-malarial drugs (sulphadoxine) and topical steroid preparations (framycetin sulphate), whose prices have accelerated 4-6 per cent annually (Table 3.1).

We next move on to investigate the price trend witnessed during this period for those drugs that were price-controlled under DPCO 1987 but decontrolled in DPCO 1995. This is very important as the drug industry continues to claim that the drug market is competitive and price rise can be checked by market

(c) Central Nervous System



(d) Anti-Tuberculosis



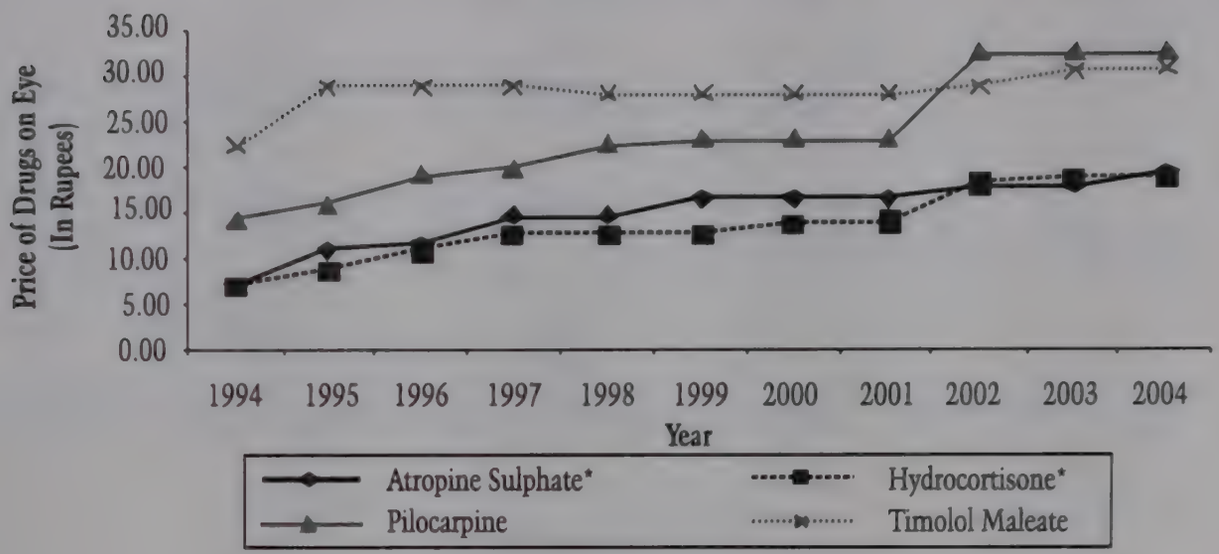
Source: Authors' calculation from *Monthly Index of Medical Specialists* (MIMS) (respective month and year), New Delhi.

forces. Does this claim actually hold up? Unlike price-controlled drugs, the general price trend of decontrolled drugs has shown an upward movement. For the 10-year period spanning 1994 through 2004, price increases have been enormous across therapeutic groups. The rise is more pronounced in the following therapeutic categories, with a double-digit price rise: antidiuretics, cardiac disorders, anti-allergic, peripheral vasodilators and antileprotics. Specifically the segments witnessing double-digit price rise are acetazolamide (18.76%), promethazine HCl (14.62%), digoxin

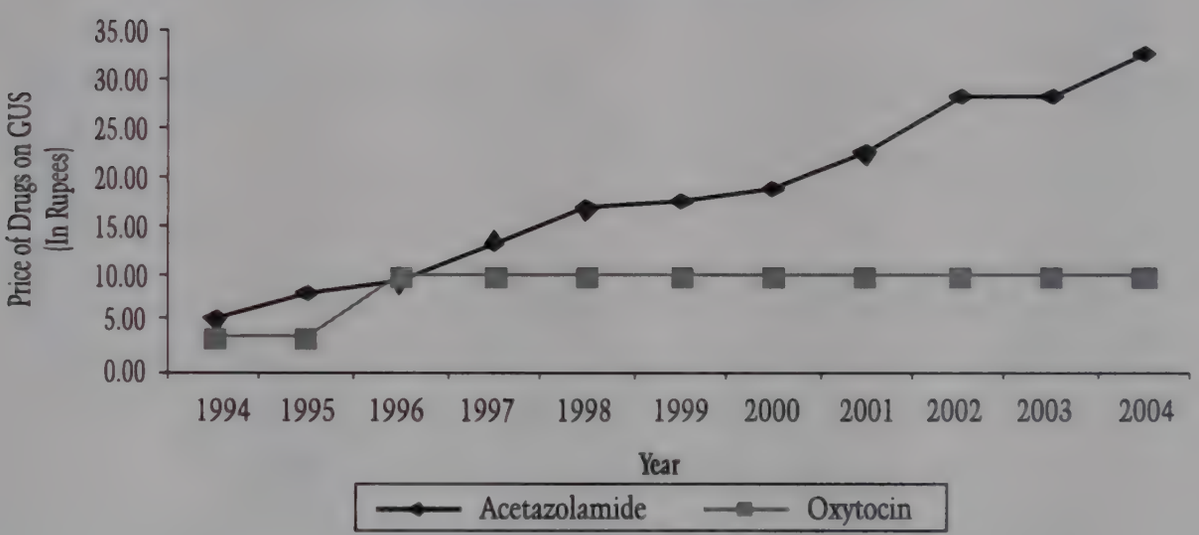
Figure 3.4(a)-(d)

Price Trends in Decontrolled Drugs, 1994-2004

(a) Drugs Relating to Eye Infections



(b) Genito-Urinary System

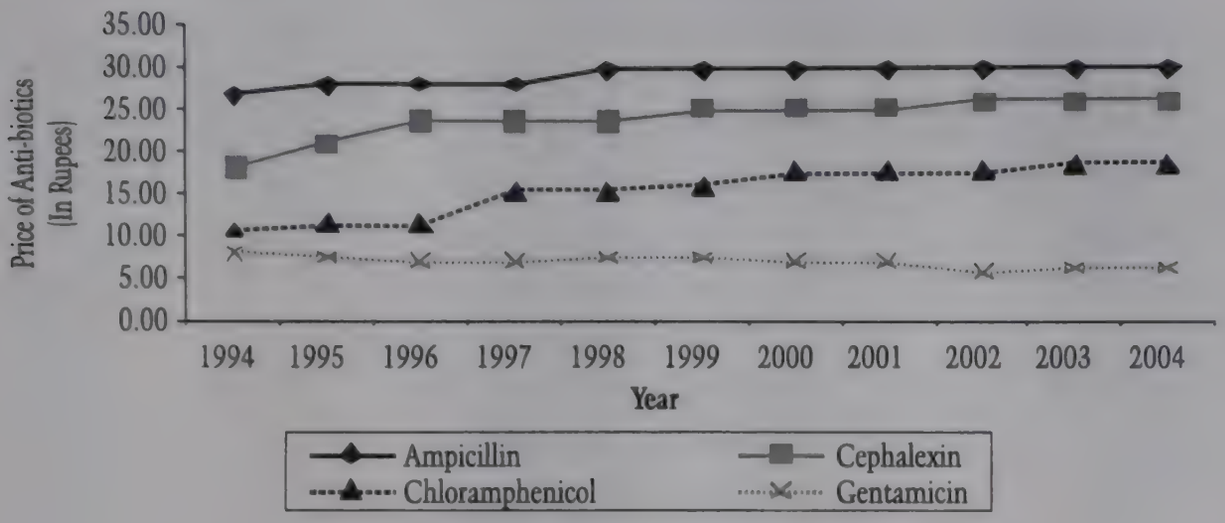


(14.38%), isoxsuprine HCl (11.35%) and clofazimine (10.84%). The antifungal preparation led by griseofulvin (0.35%) displayed price stability (Table 3.2).

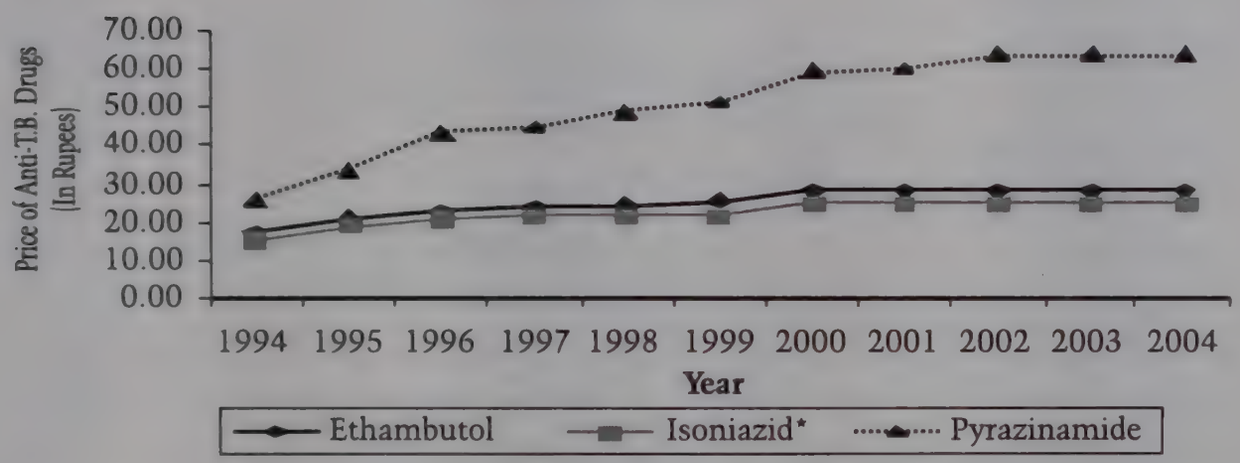
To sum up, a comparison of drug price trends (controlled and decontrolled) reveals the following:

i) Drugs under such segments as the central nervous system, cardiovascular system, genito-urinary system, respiratory system and certain sub-categories of infections and infestations like antibiotics have very clearly established that the essential drugs under control have either shown

(c) Antibiotics



(d) Anti-Tuberculosis



Source: Authors' calculation from respective years of *Monthly Index of Medical Specialists* (MIMS), New Delhi.

constant price behaviour or even declined in many categories. It must be noted, however, that there are a few exceptions to the price trends witnessed in this category. For instance, streptomycin, pentazocine, frusemide and framycetin sulphate experienced 4-6 per cent annual price rise while a couple of other formulations also witnessed a 3-4 per cent increase per annum. This could probably be attributed to the fact that the present system permits a price rise of up to 20 per cent per annum in a few exceptional cases and the companies must have exercised this option.

Table 3.1

Annual Cumulative Percentage Price Change in Price-Controlled Drugs

Therapeutic Category	*Drug*	*1994-2004*
Analgesics and antipyretics	Pentazocine	6.62
Anti-allergic drugs	Pheniramine	1.11
Antiamoebics	Griseofulvin	0.35
Antiamoebics	Metronidazole	-1.21
Antibiotics	Amikacin sulphate	-0.78
Antibiotics	Ciprofloxacin	-0.38
Antibiotics	Cloxacillin	-4.09
Antibiotics	Erythromycin	0.29
Antibiotics	Gentamicin	-1.13
Antibiotics	Tetracycline	-1.24
Anticonvulsants	Carbamazepine	-0.11
Antidiarrhoeals	Furazolidone	-2.69
Antidiarrhoeals	Nalidixic acid	-7.17
Anti-hypertensives	Methyl dopa	-1.41
Anti-hypertensives and antianginals	Verapamil	0.04
Antimalarials	Chloroquine	-3.33
Antimalarials	Sulphadoxine	4.29
Antituberculous drugs	Rifampicin	-0.66
Antituberculous drugs	Streptomycin	6.09
Bronchospasm relaxants	Salbutamol	-1.60
Bronchospasm relaxants	Theophylline	1.42
Corticosteroids and related drugs	Dexamethasone	0.00
Corticosteroids and related drugs	Prednisolone	3.75
Diuretics and antidiuretics	Frusemide	4.32
Diuretics and antidiuretics	Spironolactone	3.78
Gastro-intestinal sedatives	Ranitidine HCl	-7.44
Hyper and hypoglycaemics	Insulin	0.68
Non-steroid anti-inflammatory drugs	Ibuprofen	-1.67
Rigidity and tremor controllers	Levodopa	-5.31
Sedatives and tranquilizers	Chlorpromazine	-0.11
Topical steroid prep.	Betamethasone valerate	1.21
Topical steroid prep.	Framycetin sulphate	5.37
Urinary anti-infectives and antispasmodics	Norafloxacin	-3.19

Source: Authors' calculation from respective years of *Monthly Index of Medical Specialists* (MIMS), New Delhi.

Table 3.2

Annual Cumulative Percentage Price Change in Price-Decontrolled Drugs

Therapeutic Category	*Drug*	*1994-2004*
Analgesics and antipyretics	Paracetamol	7.03
Antacids	Aluminium hydroxide	4.16
Anti-allergic	Promethazine HCl	14.62
Antibiotics	Ampicillin	1.00
Antibiotics	Cephalexin	2.79
Antibiotics	Chloramphenicol	6.17
Anticonvulsants	Phenytoin	4.34
Antidepressants	Amitryptiline	5.02
Antidepressants	Imipramine HCl	3.23
Antidiarrhoeals	Loperamide	9.36
Antifungals	Griseofulvin	0.35
Antihelmintics and other anti-infestives	Diethylcarbamazine	8.06
Anti-hypertensives	Hydrochlorothiazide	2.06
Anti-infective prep.	Atropine sulphate	8.09
Anti-inflammatory and anti-allergic prep., and topical steroid prep.	Hydrocortisone	9.07
Antileprotics	Clofazimine	10.84
Anti-TB	Ethambutol	4.20
Anti-TB	Isoniazid	4.24
Anti-TB	Pyrazinamide	8.45
Aural prep., anti-inflammatory and anti-allergic prep., topical steroid prep.	Neomycin	1.02
Carcino-chemotherapeutic drugs	Mitomycin-C	3.85
Cardiac disorders	Digoxin	14.38
Diuretics and antidiuretics	Acetazolamide	18.76
Drugs acting on the uterus	Oxytocin	8.92
Expectorants, cough suppressant etc.	Chlorpheniramine maleate	5.68
Gastro-intestinal sedatives, anti-acid and ulcer	Metoclopramide	6.32
Glaucoma	Pilocarpine	8.17
Glaucoma	Timolol maleate	1.63
Peripheral vasodilators	Isoxsuprine HCl	11.35
Vitamins	Folic acid	4.75

Source: Authors' calculation from respective years of *Monthly Index of Medical Specialists* (MIMS), New Delhi..

ii) Essential drug prices that are now decontrolled have generally tended to move upwards marginally or in certain cases more sharply. This is revealingly captured in Table 3.2. A few products experienced a negligible price rise of 1 per cent or less, such as gentamicin, neomycin, ampicillin and griseofulvin. The presence of a large number of players in this generic market could have played a major role in stemming the price rise.

iii) The maximum price rise was observed in the category of analgesics.

iv) The drug price decline under the controlled regime has been modest, whereas the drug price rise under the decontrolled policy environment is exceedingly high.

Implications of the Proposed New Pharmaceutical Pricing Policy

Background of the Policy

After a prolonged delay since the last National Pharmaceutical Pricing Policy 2002 (NPPP 2002) was declared void by the Karnataka High Court, the Department of Pharmaceuticals under the Ministry of Chemicals and Fertilisers announced a draft National Pharmaceutical Pricing Policy 2011. NPPP 2002 attempted to reduce the number of price-controlled medicines from 76 in 1994 to 36 in 2002. Although the Supreme Court intervened in 2003 and vacated the Karnataka High Court order to stay the implementation of the 2002 Policy, the Supreme Court clearly articulated the need to consider and formulate a pharmaceutical price policy that would take into account all essential and life-saving medicines and place them under price control.

Two years after the Supreme Court verdict, the Indian government set up a Task Force to Explore Options Other Than Price Control for Achieving the Objective of Making Available Life-Saving Drugs at Reasonable Prices. The Task Force set up under the chairmanship of a former Principal Advisor to the Planning Commission, Pronab Sen, submitted its report as long ago as 2005. After that, two Groups of Ministers (UPA-I and UPA-II) under

the chairmanship of Sharad Pawar were constituted to look into the pricing issue. Their recommendations are yet to be seen, but under the pressure of a public interest litigation filed by the All India Drug Action Network in the Supreme Court, the government committed in the Supreme Court that a Drug Price Policy would be announced soon after the Health Ministry issued its latest National List of Essential Medicines (NELM). This NELM was announced in 2011 and contains 348 essential medicines. These medicines are expected to cater to the priority needs and disease burden of the vast majority of the Indian population. The essential medicines list is based on three critical factors, cost, safety and efficacy. Based on NELM 2011, the Department of Pharmaceuticals came out with a draft NPPP 2011.

Key Features of the National Pharmaceutical Pricing Policy 2011[1]

The draft NPPP 2011 will control prices of essential medicines in the following way: (i) take into consideration market-based pricing; (ii) price control only on formulations; (iii) the ceiling prices of medicines are to be regulated annually based on the wholesale price index (WPI) in order to allow manufacturers to adjust for changes in input prices; and (iv) the drugs will be excluded if the medicine price per unit is below ₹ 3.

The inclusion of all essential medicines for price control marks a departure from earlier price control regimes that relied largely on market share/dominance/monopoly elements of pharmaceutical companies. The other major departure is the intention to regulate only formulations rather than bulk drugs (APIs). The earlier price control policies aimed at regulating both formulations and bulk drugs. The most contentious issue relating to the draft NPPP 2011 is that it envisages moving to a market-based pricing mechanism as against the earlier cost-based pricing. In most markets when true competition exists, leading players reduce prices significantly (assuming no market collusion occurs) and yet obtain normal profits. However, the Indian pharmaceutical market behaves abnormally. Given that under a therapeutic category, there are

1. This section is largely derived from Selvaraj *et al.* (2012), Economic and Political Weekly.

several players with substantial variation in their prices, the prices of leading players very often tend to be the highest, because of their aggressive promotional practices and oligopolistic position. In a competitive market with complete consumer sovereignty, prices of leading players are not expected to be highest. Given the information asymmetry that creates supplier-induced demand, pharmaceutical companies have the upper hand in pushing through medicines that are high-priced. By moving to a market-based pricing mechanism, the new pharmaceutical policy attempts to legitimise the practice of rampant profiteering in the pharmaceutical market. The draft policy recommends a market-based price, which would be based on the weighted average price of three top-selling brands in each segment.

Table 3.3

Comparison of Prices of Therapeutically Similar Medicines between the Market Leader and the Cheapest Brand

Market Leader Medicine	*Active Pharmaceutical Ingredient (API)*	*TNMSC Price*	*Market Leader/ Most Expensive/ Lowest Price*	*Price Ratio of Market Leader to Lowest-Priced Brands*	*Average Price of 3 Highest-Priced Brands*	*Average Price of 3 Lowest-Priced Brands*
			Anti-Bacterial Medicines			
Monocef (1g; inj)	Ceftrixone	12.39	63 (Aristo)/ 179 (Merind)/ 45 (Neon)	1.4	125.3	50.3
Cifran (50mg; 10 tabs)	Ciprofloxacin	9.82	98.6 (Ranbaxy)/ 98.6 (Ranbaxy)/ 29.7 (Hindustan)	3.3	88.6	34.6
			Anti-Diabetics			
Amarly (1mg; 10 tabs)	Glimepride	0.75	65 (Aventis)/ 65 (Aventis)/ 9.5 (Kopran)	6.84	59.3	10.8
Glycomet GP (1mg-500mg; 10 tabs)	Metformin + glimepride	NA	36.5 (USV)/ 66.2 (Aventis)/ 17 (Blue Cross)	2.14	52.8	25.3

contd...

...contd...

Anti-Ulcer						
Omex (20mg; 10 caps)	Omeprazole	2.14	55 (Dr. Reddys)/ 79.4 (Zydus)/ 16.5 (Mankind)	3.33	51.6	20
Rantac (150mg; 10 tabs)	Ranitidine	1.85	5.98 (JB Chemicals)/ 18.9 (Cipla)/ 4.82 (Dr. Reddys)	1.25	12.7	4.9
Anti-Hypertensives						
Aten (50mg; 14 tabs)	Atenolol	1.14	38.9 (Zydus)/ 57.5 (FDC)/ 12.4 (Blue Cross)	3.14	48.8	13.2
Storvas (10mg; 10 tabs)	Atrovastatin	2.09	93.3 (Ranbaxy)/ 110 (Cadilla)/ 19 (Skymax)	4.89	103	22
Maternal and Child Health						
Methergin (0.2mg/ml; inj)	Methyl ergotamine	1.14	19.1 (Novartis)/ 19.1 (Novartis)/ 5 (M M Labs)	3.82	12.1	7.3
Zentel (400mg; 10 units)	Albendazole	4.55	17 (Glaxo)/ 17 (Glaxo)/ 7 (Bipha Labs)	2.42	16.5	7.3

Source: A variety of data sources were used. The market leader is determined based on IMS Health, 2009 data. TNMSC (Tamil Nadu Medical Services Corporation) prices are from tender prices as quoted on TNMSC websites. TNMSC prices are for a 10x10 pack, but for the sake of consistency, we have converted here into a pack of 10 tablets/capsules. Data on the three highest and lowest prices are obtained from *http://patientindia.com/resultDetails.php?searchC=1&brandId=510&genId=50&sta*

A medicine's quality should be judged not by its packaging but by its efficacy and safety. In terms of quality, lowest-priced brands are therapeutically similar to higher-priced brands of the same generic medicine. The draft policy, by choosing to fix the ceiling price based on top-selling brands, is legitimising the trend of high prices. This will induce players in the currently lower-priced segment to drive up prices closer to the higher-priced medicines.

Table 3.3 provides a snapshot view of the prevailing market conditions and associated prices across various therapeutic categories. Prices of the leading market players are the ones that are often highest. The ratio of market leader prices to the prices of the cheapest brands is in the range of 1.25 to 6.84. It is also interesting

to observe that the tender prices (as for the Tamil Nadu Medical Services Corporation) in several instances are much lower than even the average of the three lowest prices in the market. This clearly shows that several players are making more than normal profit, even when their prices are lowest among companies selling the same generic medicine.

Further, the draft policy states: "The Bulk Drug—API (Active Pharmaceutical Ingredient)—may not fully reflect the 'Essentiality' of the actual drug formulation—now the subject of focus—due to the possible applicability of the API in manufacture of various formulations which may or may not be considered 'Essential' for the larger health care needs of the masses." This effectively means that companies will be allowed to make inessential formulations from essential bulk drugs and these formulations would fall outside price control even if the basic single-ingredient medicine comes under the price control list because it is included in NLEM 2011. Typically companies would misuse this provision by reducing production of single-ingredient essential medicines and would manufacture inessential or irrational combinations using essential medicines. We already have a situation where a very large number of irrational formulations exist in the market. Given the therapeutic jungle that India has entered, with over 92,000 brands existing in the market, the policy will accelerate the proliferation of irrational drugs and lead to a shortage of essential single-ingredient medicines.

The naïve faith in markets that pervades the current political economy and policy-making is clearly reflected in the draft NPPP 2011. The draft policy argues: "The Indian economy is today largely market-driven and, particularly in the area of pricing of manufactured products, prices are determined by market conditions and market forces. Administered prices exist in a few areas, such as pricing of petroleum products and procurement prices of food-grains but these are closely connected with a regime of subsidies paid by the Government. The Pharmaceutical Industry is a 1 lakh crore [₹ 1 trillion] industry of which about ₹ 48,200 crores [₹ 482 billion] is the domestic market." Apparently, what is important for the policy is to safeguard the interests of the ₹ 1 lakh crore industry, not the 40 million people who are pushed below the poverty line and

an equal number of people who incur catastrophic payments due to high medicine prices (Selvaraj and Karan, 2009). The policy patently disregards the acute financial barriers to access to medicines.

The draft NPPP 2011 stipulates that essential medicines whose weighted average price is less than or equal to ₹ 3 per unit would be exempted from price control. If this is carried out, it will give the manufacturers leeway to increase the prices of dozens of essential medicines which are currently available at prices far below ₹ 3 per unit (including many painkillers, anti-inflammatory agents, anti-histamines, anti-asthmatics, some anti-diabetics, anti-hypertensives etc.).

Another major limitation of the proposed price control as envisaged in the draft policy is that it would limit itself to controlling the prices of only those medicines in the NLEM 2011 list. NLEM 2011 itself should be subject to a thorough review as it appears to omit critical medicines that the government itself provides in its treatment programmes. There appears to have been too much reliance on the "cost" factor in determining NLEM 2011, raising the question of how key patented medicines will be dealt with under the NPPP. With the draft NPPP 2011 limiting itself to NLEM 2011 in terms of price control, this has the potential of setting off a vicious cycle where patented medicines will remain out of the ambit of price control and, being costly, will have little chance of being included in the NLEM. The draft NPPP 2011 is therefore incomplete and only partially addresses the problem of affordability and access to medicines.

The draft NPPP 2011 disregards the fact that it is not enough to bring only one medicine under price control out of the range of medicines in the category to which the medicine belongs. For example, out of a range of medicines in the category of ACE-inhibitors (used for the treatment of high blood pressure), it is not enough to single out only enalapril to bring it under price control. All other ACE-inhibitors (lisinopril, ramipril, perindopril) should also be under price control. Though there is hardly any difference amongst these four medicines as regards efficacy, side-effects etc., there is a significant price difference between enalapril and others. The generic version of enalapril 5 mg costs less than ₹ 5 per strip of

10 tablets while its branded version costs around ₹ 25. In contrast, the branded versions of lisinopril, ramipril and perindopril, for an equivalent dosage, are priced at ₹ 38, ₹ 67 and ₹ 79 respectively per strip. If all ACE-inhibitors are not under price control, pharmaceutical companies would mislead and entice doctors into prescribing the three costly ACE-inhibitors. Hence, such "me too" drugs should have the same price ceiling, namely, the ceiling of the therapeutically similar drug.

Policy Options

The draft NPPP 2011 falls far short of the goal of ensuring accessibility and affordability of medicines in India, both in terms of scope, by addressing only the medicines in NLEM 2011, and in terms of its market-based approach. The industry and the government complain that cost-based pricing is difficult to administer since pharmaceutical companies are not mandated to declare the true cost of producing medicines. A proxy way to get around this problem is to obtain tender prices (as in Tamil Nadu or Kerala) and treat these as reference prices. The retail price can then be calculated by adding a suitable margin to the reference price. Given the unique but distorted nature of the pharmaceutical market, reference prices based on lowest, rather than highest, prices are the way forward. By fixing reference prices, the government can give a signal to the industry that adequate margins are allowed, which will be above normal profit. Contrary to dire threats by the industry, such pricing will keep them engaged in the business of making medicines. Despite price controls in the past, the industry has consistently registered super-normal profits. Even if floor-plus prices were to be considered, they would reap above normal profits.

Cost-based pricing could have been possible if the government had allowed the pharmaceutical public sector undertakings (PSUs) to function smoothly and efficiently. Over the years, however, the government has let them decline, foregoing a golden opportunity for robust benchmarking. The revival of the pharmaceutical PSUs, therefore, is extremely important. It is also important to revive the PSUs for other reasons. If the government issues a compulsory licence for a patented product, the pharmaceutical PSUs would need

to operationalise the licence. Moreover, in an environment where the top Indian private pharmaceutical companies are being acquired by multinational drug companies or have licensing arrangements with them, PSUs need to play a significant role in providing medicine security.

The Department of Pharmaceuticals must be required to continuously collect and disseminate pharmaceutical market data, such as market share, consumption pattern and prices, which is currently being done by a private data collecting agency (like IMS Health). The prohibitive cost of obtaining this data from a private agency makes independent evaluation by health and public interest groups an impossible task. Such data should be available in the public domain, and it is well within the powers of the government under the Essential Commodities Act to gather and disseminate such data.

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BISWAJIT DHAR and REJI K. JOSEPH

Recent Performance of the Indian Pharmaceutical Industry

The Indian pharmaceutical industry has evolved over three phases. The first was the period prior to 1970, when the industry was dominated by a few foreign-owned and foreign-controlled firms.[1] The second phase, from the second half of the 1970s to the early 1990s, was a period during which the industry experienced structural transformation through the growth of the Indian generic drug industry. This development was a result of the adoption of the Patents Act of 1970. The Indian government introduced two changes in the country's patent regime—introduction of a process patent regime and shortening the term of pharmaceutical patents—both of which had considerable impact in shapingthe pharmaceutical industry in India. Firms belonging to Indian promoters began to take root in the industry during the 1970s, and by the 1990s, these firms had consolidated their position in the industry.[2]

The Indian pharmaceutical industry thus developed has a three-tier structure. It consists of a large private sector,[3] which can be further divided into two categories of firms, that is, firms that

1. In India, a distinction was made between 'foreign-owned' and 'foreign-controlled' firms. 'Foreign-owned' firms were those in which non-residents had majority in the equity (voting) shares. 'Foreign-controlled' firms were identified by the Reserve Bank of India (RBI) as those firms in which non-residents' equity (voting) shares were 26 per cent or more.

2. For a discussion on the evolution of the Indian pharmaceutical industry, see Dhar and Rao (2002).

3. In the earlier decades, public sector firms, or government-promoted firms, were set up, essentially with the objective of producing the bulk drugs or the active ingredients. These firms went out of business after market-oriented reforms were initiated in the early 1990s.

are affiliates of foreign firms in India[4] and those that have Indian promoters and produce generic drugs, and the small-scale units.

Yet another way of looking at the Indian pharmaceutical industry is to characterise it in terms of the scale of operation of the units. From this perspective, the Indian pharmaceutical industry can be characterised as 'long-tailed,' that is, there are a relatively small number of large firms and a large number of small firms.[5]

The performance of the pharmaceutical industry can be seen by analysing data that are available only with respect to the large firms.[6] One of the limitations of these data is that firms belonging to the small-scale sector are not represented, since most of them are not public limited firms. It must be stated, however, that focusing the analysis on the larger firms provides one distinct advantage—it helps in understanding the broad trends in the Indian pharmaceutical industry. This advantage is reinforced by the fact that the large firms have an overwhelming presence in the industry. Data available for the top 23 firms, which account for 80 per cent of the net worth of the pharmaceutical industry in 2008-2009—5 of which operate in India as affiliates of foreign firms,[7] with the remaining 18 having Indian promoters[8]—provide evidence in this regard. For our analysis, we focus on the performance of these 23 firms indicated above.

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4. The foreign-owned and foreign-controlled firms were forced to 'Indianise' by diluting their foreign equity holding in the beginning of the 1970s. As a result, most of these firms became 'foreign-controlled,' which, according to the RBI, were firms having more than 26 per cent foreign equity holding.

5. In the year 2000, the latest year for which the Indian government provided data on the number of units involved in pharmaceutical production in India, it was reported that "about 250 large units and about 8,000 small scale units [are] in operation." See Government of India (GoI) (2000).

6. Most of these firms are public limited firms and their financial data, in particular, are in the public domain. The data that we have used were obtained from the Prowess database of the Centre for Monitoring Indian Economy (CMIE).

7. The following are firms with foreign affiliations currently operating in India: Ranbaxy, GlaxoSmithKline Pharmaceuticals Ltd., Aventis Pharma Ltd., Pfizer Ltd. and Matrix Laboratories Ltd.

8. The 18 major firms of Indian origin are: Dr. Reddy's Laboratories Ltd., Cipla Ltd., Sun Pharmaceutical Inds. Ltd., Wockhardt Ltd., Cadila Healthcare Ltd., Lupin Ltd, Orchid Chemicals & Pharmaceuticals Ltd., Biocon Ltd., Divi's Laboratories Ltd., Glenmark Pharmaceuticals Ltd., Piramal Healthcare Ltd., Torrent Pharmaceuticals Ltd., Plethico Pharmaceuticals Ltd., Ipca Laboratories Ltd., Panacea Biotech Ltd., Dishman Pharma Ltd., JB Chemicals and Pharmaceuticals Ltd. and Unichem Laboratories Ltd.

The 1990s was an important decade for it saw the Indian pharmaceutical industry performed strongly on all fronts. Total production of the industry (large firms and the small-scale units taken together) expanded more than fourfold in value terms (in domestic currency). The dollar value of exports too registered a similar increase. There is strong evidence that the Indian industry was getting increasingly outward-oriented—the share of exports in total production almost doubled during the decade (Dhar and Rao, 2002).

But it was in the post-1995 phase that the large firms in the industry performed strongly on all fronts. During this phase, the leading generics producers were relatively more active as compared to the leading firms that are affiliates of foreign firms. This is evidenced by the fact that while in 1994-95, five of the top 10 pharmaceutical firms (in terms of sales turnover) were foreign affiliates, in 2008-09, GlaxoSmithKline and Matrix were the only two foreign affiliates in the top 10 list. It is interesting that this robust performance by the Indian pharmaceutical firms, in particular the generics segment of the industry, has come during a phase when they were facing an uncertain future, with the process patent regime being dismantled following India's accession to the World Trade Organization (WTO). The following discussion provides the evidence in support of the above-mentioned point.

The first indicator for analysing the performance of the pharmaceutical industry is the net worth of the firms, which is a reflection of their respective market values. Table 4.1 provides the details.

It is evident from Table 4.1 that most of the generics manufacturers consolidated their positions in the industry. The larger among them, such as Dr. Reddy's, Sun and Cipla, show very high rates of growth in net worth during the 15-year period from 1994-95 to 2008-09. Interestingly, relatively smaller firms, such as Dishman, Panacea, Plethico, Biocon and Divi's, experienced higher growth as compared to the larger ones during the same period.

Table 4.1

Annual Growth in Net Worth of Leading Firms in the Indian Pharmaceutical Industry

Company	*Net Worth in 2008-09 ($ million)*	*Growth Rate**			
		1994-95 to 2008-09	*1994-95 to 1999-2000*	*2000-01 to 2004-05*	*2005-06 to 2008-09*
Dr. Reddy's Laboratories Ltd.	1,145.4	19.6	4.3	30.6	22.4
Sun Pharmaceutical Inds. Ltd.	1,121.9	27.3	18.9	19.2	35.7
Cipla Ltd.	947.5	25.7	27.8	16.8	20.6
Ranbaxy Laboratories Ltd.	880.0	10.2	9.6	8.4	13.6
GlaxoSmithKline Pharmaceuticals Ltd.	383.0	14.0	8.0	17.2	16.1
Lupin Ltd.	299.5	23.5	3.3	7.1	19.8
Biocon Ltd.	299.4	39.8	0.0	60.2	13.4
Divi's Laboratories Ltd.	274.8	33.5	9.6	25.4	37.5
Cadila Healthcare Ltd.	268.5	9.4	70.2	2.7	12.7
Glenmark Pharmaceuticals Ltd.	267.9	28.3	47.3	17.6	38.9
Piramal Healthcare Ltd.	259.0	9.8	5.0	6.2	4.3
Pfizer Ltd.	223.5	19.5	8.7	19.0	27.8
Aventis Pharma Ltd.	206.0	11.3	1.0	15.1	15.3
Matrix Laboratories Ltd.	191.1	19.9	-27.3	114.9	-0.7
Wockhardt Ltd.	168.3	12.1	2.8	17.5	-1.5
Torrent Pharmaceuticals Ltd.	159.6	10.7	8.4	7.5	16.6
Plethico Pharmaceuticals Ltd.	151.5	29.4	10.6	24.9	26.9
Orchid Chemicals & Pharmaceuticals Ltd.	146.0	12.2	22.1	3.8	-4.7
Ipca Laboratories Ltd.	139.1	10.1	2.3	14.3	12.4
Panacea Biotec Ltd.	134.0	32.4	42.0	21.5	24.0
Dishman Pharmaceuticals & Chemicals Ltd.	120.6	42.6	0.0	46.5	32.8
JB Chemicals & Pharmaceuticals Ltd.	115.9	14.9	13.0	12.7	11.4
Unichem Laboratories Ltd.	113.2	15.5	4.6	15.8	13.6
For the 23 firms	*8,015.5*	*18.0*	*14.6*	*16.2*	*18.1*
For the pharmaceutical industry as a whole	*9,979.5*	*12.3*	*8.7*	*13.2*	*11.6*

Note: * Compound annual growth rate.

Source: Prowess database of the CMIE.

The data presented in Table 4.1 also indicate that barring a couple of exceptions, firms that are affiliates of foreign firms increased their stakes in the Indian industry. More importantly, these firms increased their stakes at a much faster rate during the recent past as compared to the second half of the 1990s. This tendency was prominently displayed by Pfizer, with the firm having consolidated its position to emerge as the largest firm in this group after GlaxoSmithKline Ltd.

Ranbaxy, the top performer in the Indian pharmaceutical sector which was taken over by a multinational company, Daiichi Sankyo, in 2008, was the largest firm in the pharmaceutical sector till a few years back, but did not experience a comparable increase in market value. Similarly Matrix, another Indian firm taken over by a multinational company, has shown negative growth in the last few years.

Major Indian as well as foreign firms have been engaging in mergers and acquisitions to consolidate their positions. For example, Matrix had taken control of 10 Indian firms through mergers and takeovers during the period from 2001 to 2007.[9] Indian generics firms have also been actively engaging in mergers and acquisitions. Thus, Ranbaxy had taken control of 10 firms, Sun seven, Cipla five and Dr. Reddy's four during the period from 1995 to 2007.

Another major feature of the Indian pharmaceutical industry is that the bio-pharma sector is becoming an important segment. Biocon, the largest bio-pharma firm in India, ranks seventh in the list of top 23 firms and was second in terms of growth in net worth during the period from 2000-01 to 2004-05. Another major bio-pharma firm, Panacea, shows a growth rate of 24 per cent during the last four years, which is much higher than the average of 18.1 per cent for all 23 firms.

Further evidence of the strength of the generics manufacturers in the Indian pharmaceutical industry is available from the market penetration these firms achieved from 1994-95 to 2008-09. Table

9. The 10 firms are Dolphin Drugs Pvt. Ltd., Medicon Pharmaceuticals Pvt. Ltd., Medicorp Technologies India Ltd., Vorin Laboratories Ltd., Vera Laboratories Ltd., Calibre Engineering Pvt. Ltd., Medikon Laboratories Pvt. Ltd., United Intermediates & Chemicals Pvt. Ltd., Concord Biotech Ltd. and Fine Drugs & Chemicals Ltd.

4.2 shows that the generics firms recorded sales growth which far outstripped that registered by the associates of foreign firms in India.

Table 4.2

Annual Growth in Sales of Leading Firms in the Indian Pharmaceutical Industry

Company	*Sales in 2008-09 ($ million)*	*Growth Rate**			
		1994-95 to 2008-09	*1994-95 to 1999-2000*	*2000-01 to 2004-05*	*2005-06 to 2008-09*
Cipla Ltd.	1,153.7	18.1	11.0	18.0	13.3
Dr. Reddy's Laboratories Ltd.	986.9	20.1	10.4	10.8	19.3
Ranbaxy Laboratories Ltd.	977.2	10.2	9.7	15.5	7.5
Lupin Ltd.	652.0	29.6	2.3	8.8	13.9
Sun Pharmaceutical Inds. Ltd.	617.1	23.3	26.7	13.6	19.2
Piramal Healthcare Ltd.	519.9	16.9	14.7	18.3	11.1
GlaxoSmithKline Pharmaceuticals Ltd.	447.1	3.9	-2.6	8.1	6.0
Cadila Healthcare Ltd.	388.0	15.2	13.8	19.2	6.4
Wockhardt Ltd.	361.1	14.1	33.2	8.3	15.0
Matrix Laboratories Ltd.	327.6	34.4	17.8	58.3	16.5
Ipca Laboratories Ltd.	291.8	10.8	5.4	13.5	12.0
Aventis Pharma Ltd.	266.0	6.8	3.9	12.3	8.3
Divi's Laboratories Ltd.	262.2	23.4	19.3	13.7	31.0
Orchid Chemicals & Pharmaceuticals Ltd.	262.0	21.6	34.7	13.5	7.1
Torrent Pharmaceuticals Ltd.	258.9	8.7	4.8	6.8	11.4
Biocon Ltd.	204.5	25.2	0.0	41.4	5.7
Pfizer Ltd.	195.5	6.3	0.3	11.5	5.0
Glenmark Pharmaceuticals Ltd.	190.3	18.7	14.2	23.1	7.9
Panacea Biotec Ltd.	169.8	18.2	21.6	8.3	8.2
JB Chemicals & Pharmaceuticals Ltd.	152.0	10.4	2.8	9.8	8.8
Unichem Laboratories Ltd.	144.6	9.3	3.8	11.4	7.6
Plethico Pharmaceuticals Ltd.	118.7	20.8	17.9	11.5	24.2
Dishman Pharmaceuticals & Chemicals Ltd.	92.3	23.1	0.0	18.1	16.9
For 23 firms	*9,039.1*	*14.8*	*11.1*	*14.5*	*12.1*
For pharmaceutical industry as a whole	*12,575.0*	*8.3*	*6.9*	*10.3*	*2.8*

Note: * Compound annual growth rate.

Source: Prowess database of the CMIE.

The growth in sales registered by the leading generics producers led to a complete transformation of the composition of market leaders in the Indian pharmaceutical industry. In 1994-95, five of the 10 top firms in terms of sales were associates of foreign firms, with GlaxoSmithKline (then Glaxo India Ltd.) as the market leader. But in 2008-09, nine of the top 10 sellers were generics firms, and GlaxoSmithKline was only the seventh largest firm in terms of sales. Matrix, though taken over by a foreign firm, continues to be a prominent generics firm.

There has been an interesting transformation in the constitution of the top five firms over the last 15 years. In 1994-95, the top five were constituted by three multinational corporations (MNCs) (Glaxo, Novartis and Aventis) and two generics firms (Ranbaxy and Cipla), with Glaxo being ranked first. By 2005-06, this group comprised four generics firms (Ranbaxy, Dr. Reddy's, Cipla and Lupin) and one MNC (Glaxo), with Ranbaxy at the top. And in 2008-09, this group constituted only generics firms and Ranbaxy was pushed to third position. Cipla, the market leader, is the only firm to cross the $1 billion sales benchmark. Its sales have multiplied by more than 12 times over the last 15 years. Dr. Reddy's and Ranbaxy are close to reaching the $1 billion benchmark.

It is seen from Table 4.2 that these 23 firms are performing very well in terms of growth as compared to the industry as a whole. A significant number of firms registered double-digit growth in sales in the last four years. How do these booming sales translate to profits? Table 4.3 gives the profit data.

Most of the firms listed in the table exhibit double-digit profitability figures. Most of the companies have shown a progression in profitability, defined as percentage of sales, from the 1990s to the first half of this decade to the last four years. What is striking is that the difference between the profitability ratios of the leading generics firm and the leading MNC is narrowing and in the last four years the profitability of the leading MNC (GlaxoSmithKline) has outpaced that of the leading generics firm (Sun). In the 1990s also, these were the leading firms in the two categories and Sun was leading in profitability by more than 10 percentage points.

Table 4.3

Profitability Ratios of the Leading Firms in the Indian Pharmaceutical Industry

Company	*Profit Before Tax, 2008-09 ($ million)*	*Profit as Percentage of Sales*			
		1994-95 to 2008-09	*1994-95 to 1999-2000*	*2000-01 to 2004-05*	*2005-06 to 2008-09*
Sun Pharmaceutical Inds. Ltd.	282.1	30.4	24.5	29.3	40.6
GlaxoSmithKline Pharmaceuticals Ltd.	200.8	22.8	13.5	17.8	43.2
Cipla Ltd.	196.3	20.1	19.5	20.5	20.4
Dr. Reddy's Laboratories Ltd.	158.9	18.3	16.9	19.1	19.4
Lupin Ltd.	107.5	11.9	10.4	9.2	17.4
Pfizer Ltd.	104.0	18.6	10.1	14.7	36.3
Divi's Laboratories Ltd.	100.6	24.6	8.0	23.9	33.6
Piramal Healthcare Ltd.	72.5	12.5	11.4	12.2	14.5
Cadila Healthcare Ltd.	64.6	12.3	8.1	13.3	15.4
Aventis Pharma Ltd.	64.5	15.6	7.9	17.4	24.9
Matrix Laboratories Ltd.	56.6	8.1	0.7	17.3	7.8
Torrent Pharmaceuticals Ltd.	45.8	14.3	12.3	15.6	15.7
Glenmark Pharmaceuticals Ltd.	41.3	16.1	14.2	12.6	22.9
Unichem Laboratories Ltd.	31.4	11.6	5.7	12.6	19.1
Biocon Ltd.	28.5	24.0	0.0	22.1	26.3
Ipca Laboratories Ltd.	26.0	10.1	7.4	11.5	12.4
Dishman Pharmaceuticals & Chemicals Ltd.	22.9	19.7	0.0	16.4	22.2
JB Chemicals & Pharmaceuticals Ltd.	21.3	14.8	11.9	18.9	14.0
Plethico Pharmaceuticals Ltd.	15.8	22.3	15.3	22.2	24.1
Orchid Chemicals & Pharmaceuticals Ltd.	-8.0	9.7	13.4	5.5	9.5
Panacea Biotec Ltd.	-20.1	11.8	9.8	12.8	13.5
Wockhardt Ltd.	-113.6	17.0	20.3	18.6	11.6
Ranbaxy Laboratories Ltd.	-401.3	11.9	15.4	16.9	0.5
For 23 firms	*1,098.2*	*16.1*	*13.5*	*16.8*	*19.3*
For pharmaceutical industry as a whole	*1,378.75*	*10.7*	*7.4*	*11.3*	*15.1*

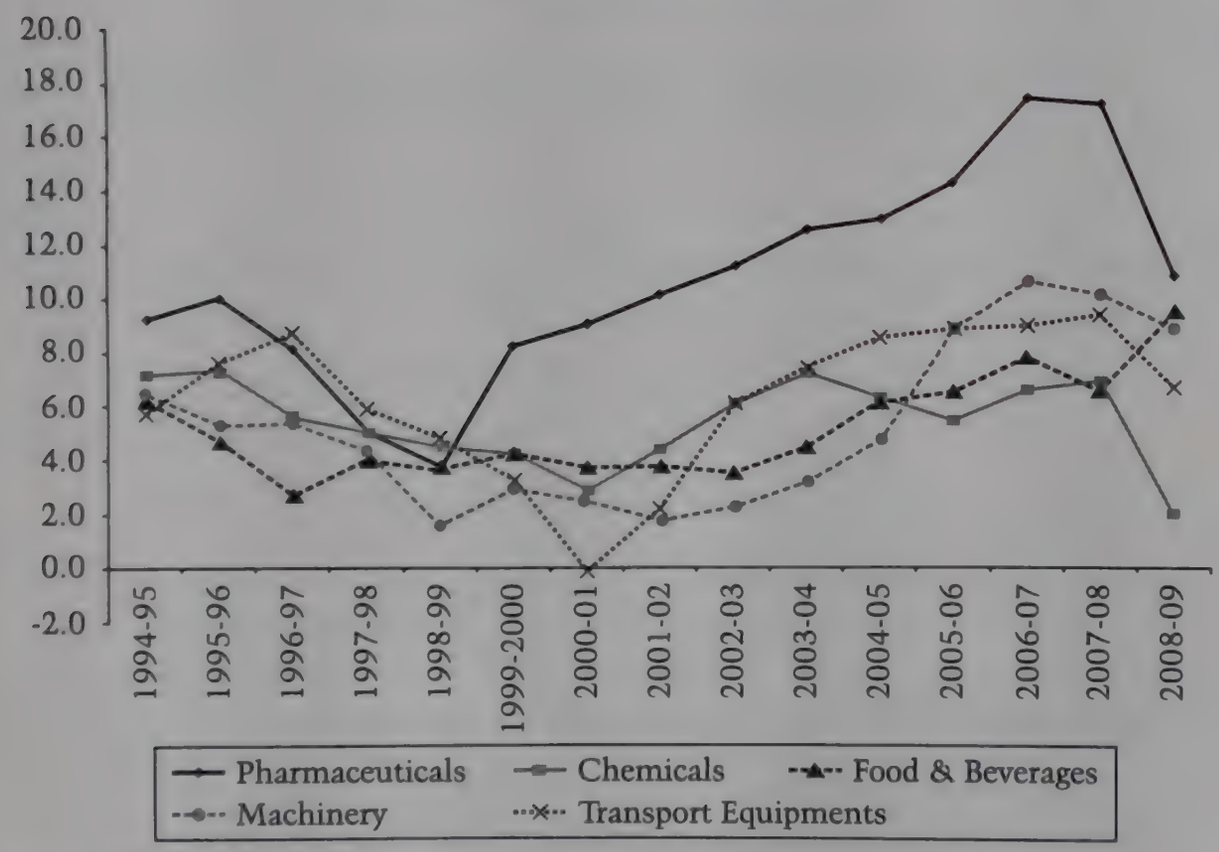
Source: Prowess database of the CMIE.

We also observe that there is a leap in the profitability of major MNCs GlaxoSmithKline and Pfizer in the post-2005 period. The profitability of GlaxoSmithKline increased by some 25 percentage points and that of Pfizer by 22 percentage points in the post-2005 period as compared to the previous five years. Thus it appears that the profitability of major MNCs recorded a quantum leap with India amending its patent regime to provide for product patent rights in pharmaceuticals and agro-chemicals.

A noteworthy feature of the pharmaceutical sector is that it is the most profitable among all the leading sectors of Indian industry. Interestingly, the profitability ratio of the pharmaceutical industry increased almost consistently through the period (see Figure 4.1). It needs to be reiterated here that the pharmaceutical industry had outperformed other sectors of industry despite facing an additional dose of uncertainty arising from the changes in the patent regime.

Figure 4.1

Profitability (Profit Before Tax as Percentage of Sales) across Different Sectors in India



Source: Prowess database of the CMIE.

The global integration of the Indian economy, which many sectors of the economy considered as a threat, opened a wide

Table 4.4

Ratio of Exports to Sales

(Per cent)

Company	*1994-95*	*1996-97*	*1998-99*	*2000-01*	*2002-03*	*2004-05*	*2006-07*	*2008-09*
Divi's Laboratories Ltd.	0.0	0.0	86.6	85.5	84.6	81.9	90.7	91.7
Matrix Laboratories Ltd.	14.6	10.5	3.8	6.7	67.6	50.7	64.4	81.4
Orchid Chemicals & Pharmaceuticals Ltd.	98.6	94.3	87.7	85.7	82.5	75.4	75.0	77.5
Dishman Pharmaceuticals & Chemicals Ltd.	0.0	0.0	0.0	0.0	88.0	66.3	68.0	72.8
Ranbaxy Laboratories Ltd.	41.5	48.7	37.8	42.4	56.7	60.4	71.9	68.2
JB Chemicals & Pharmaceuticals Ltd.	20.9	40.6	31.3	42.6	46.5	52.4	52.6	64.2
Dr. Reddy's Laboratories Ltd.	32.2	28.0	27.8	43.1	57.2	55.8	67.9	63.8
Plethico Pharmaceuticals Ltd.	0.0	0.0	0.0	18.6	7.7	63.6	57.6	56.1
Lupin Ltd.	0.0	0.0	0.4	27.7	39.8	44.5	45.2	52.8
Cipla Ltd.	10.4	13.6	18.7	24.3	36.0	43.9	48.7	51.8
Biocon Ltd.	0.0	0.0	0.0	21.1	39.0	54.6	50.5	49.3
Ipca Laboratories Ltd.	32.9	42.8	44.3	41.4	51.2	53.3	47.3	49.1
Cadila Healthcare Ltd.	0.0	9.1	8.7	12.4	10.5	12.0	19.1	36.1
Wockhardt Ltd.	0.0	11.4	20.4	21.0	30.7	34.9	33.6	36.0
Sun Pharmaceutical Inds. Ltd.	5.1	5.2	17.4	20.3	17.8	26.3	27.9	28.7
Torrent Pharmaceuticals Ltd.	0.0	2.3	8.8	7.2	9.3	15.0	18.4	27.8
Panacea Biotec Ltd.	4.1	6.5	9.2	6.7	4.3	4.0	18.8	24.1
Piramal Healthcare Ltd.	5.9	8.0	0.7	0.1	3.4	9.6	16.7	23.8
Glenmark Pharmaceuticals Ltd.	0.0	6.4	0.0	5.2	5.4	24.0	36.2	23.7
Unichem Laboratories Ltd.	5.9	3.5	4.0	5.9	7.5	14.0	20.8	20.6
Aventis Pharma Ltd.	12.7	20.0	12.2	10.7	19.1	24.3	23.2	19.2
GlaxoSmithKline Pharmaceuticals Ltd.	2.5	3.5	7.4	7.6	5.0	1.9	1.8	3.3
Pfizer Ltd.	1.8	1.1	2.6	0.6	0.8	0.5	0.2	0.2

Source: Prowess database of the CMIE.

window of opportunity for the generic pharmaceutical industry. This was because the leading firms in this segment of the industry were considerably more outward-oriented as compared to those in other industries. The trend towards enhancing the outward orientation of the industry had begun in the early 1990s and went through a rapid consolidation in the subsequent years. This was particularly noticeable in the case of the large generics firms in the industry. Table 4.4 shows that for the three largest firms in this segment, Ranbaxy, Dr. Reddy's and Cipla, exports in terms of value were more than one-half of their sales turnovers. For some smaller firms, for example Divi's, exports constitute more than 90 per cent of sales. For these firms, therefore, foreign markets were relatively more important than the domestic market and this gave them the impetus to improve their operating efficiencies.

Foreign firms operating in India do not engage significantly in exports, as indicated by their ratio of exports to sales; their production capacities in the country are increasingly being used for satisfying domestic demand. This tendency stands out particularly prominently in larger firms in the global industry such as GlaxoSmithKline and Pfizer. Pfizer has had a very low export ratio since the beginning and GlaxoSmithKline reduced its exports since the middle of the decade. This, in other words, implies that the global pharmaceutical majors did not show much interest in converting their production facilities in India into manufacturing hubs from which they would like to supply to the global market. Generics producers Matrix and Ranbaxy, though affiliates of foreign firms, show very high export intensity.

The strong performance of the generics industry in the global market resulted from a number of its inherent advantages. It has been argued that Indian firms have lower costs—estimated to be one-eighth in research & development (R&D) activities and one-fifth in manufacturing—as compared to the Western firms (Grace, 2004). The cost advantages are most pronounced in respect of lower fixed asset costs and labour costs, where the costs in India can be one-eighth of the cost in the US.

Table 4.5

Share of Exports of Generic Formulations: Region-wise

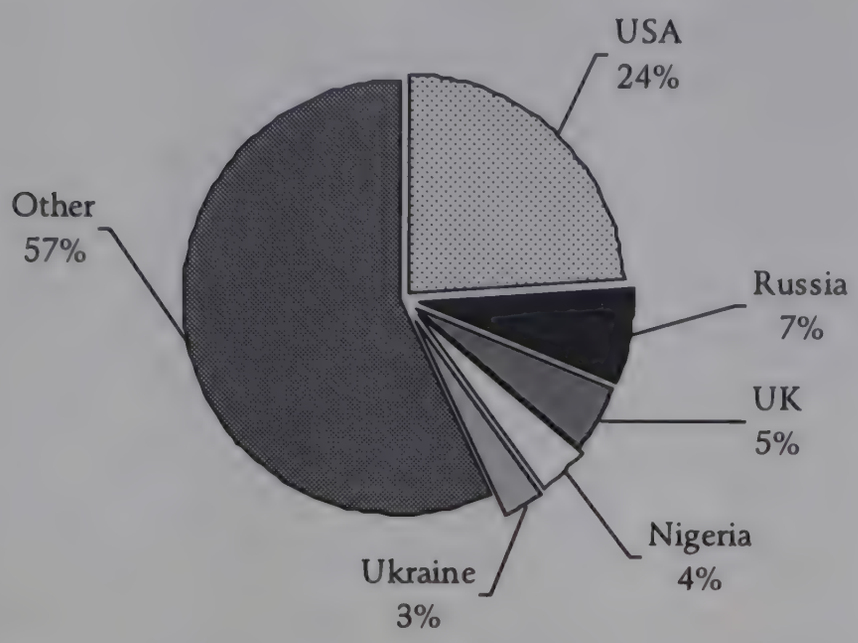
	Africa	*Americas*	*Asia*	*Europe*	*Oceania*
1994-95	17	7	32	44	1
1995-96	17	9	32	41	1
1996-97	16	9	33	40	1
1997-98	18	10	32	39	1
1998-99	22	13	37	27	1
1999-2000	20	11	37	30	1
2000-01	23	15	32	30	1
2001-02	24	20	28	27	1
2002-03	23	24	25	26	1
2003-04	22	22	27	28	1
2004-05	21	21	25	31	1
2005-06	23	21	23	32	1
2006-07	23	27	20	29	1
2007-08	22	32	17	27	1

Source: Directorate General of Commercial Intelligence and Statistics (DGCIS).

Table 4.5 shows the trends in exports of generic formulations across different regions. In 1994-95, more than three-fourth of the exports of formulations were destined to Europe and Asia. By 2007-08, the share of these two regions had declined to 44 per cent. This decline was not because of a drop in the value of exports but rather the expansion of exports to other regions. The decline in the share of Europe and Asia was offset by the expansion in exports to other regions, especially to the Americas and Africa. Now, the Americas is the region accounting for the single largest share in exports (32%). Exports to the Americas have grown from a mere $3.7 million in 1990-91 to $1,097.5 million in 2007-08. The US accounts for three-fourth (76% in 2007-08) of exports destined to the Americas. The share of Africa has increased from 5 per cent in 1990-91 to 22 per cent in 2007-08. In the case of Asia, there was an increase in its share in the 1990s but it declined in the subsequent decade, rising from 13 per cent in 1990-91 to 37 per cent in 1999-2000 before declining to 17 per cent in 2007-08.

Figure 4.2

Top Five Destination Countries in the Export of Formulations, 2007-08



Source: DGCIS.

Figure 4.2 shows the top five export destination countries of formulations. The 'low volume high value' market of the US remains the main attraction for formulation exporters. India has approximately 119 FDA (US Food and Drug Administration)-approved plants,[10] the largest number outside the US and approximately twice the amount that China presently has. Recent market estimates indicate that there would be further acceleration of Indian exports to the US. It is estimated that about 250 Indian generic products have been launched in the US market in 2008, as opposed to 93 in 2003.[11] It is estimated that in the US, $40 billion worth of drugs are expected to go off-patent in the coming years.[12] Up until the end of the 1980s, Indian firms focused extensively on the other world markets, especially the USSR where there was little patent protection coupled with lax registration requirements. The accumulation of enhanced technologies and production capabilities coupled with the change in the global patent regime led to a gradual

10. See Department of Commerce, Govt. of India (2008).
11. KPMG (2006). "The Indian Pharmaceutical Industry: Collaboration for Growth," p.9 in Padmashree G. Sampath (2008).
12. See Department of Commerce, Govt. of India (2008).

shift of focus to the highly lucrative US generics market while retaining the old markets.

To market a generic drug in the US, a company needs to file an Abbreviated New Drug Application (ANDA). When filing an ANDA, the company is required to certify that its product is not infringing any patent rights or the patent is invalid (para IV certification). If the company successfully proves that the patent is invalid or if it is the first one to get approval for the generic version, it gets market exclusivity for 180 days during which no other generics company is permitted to enter the market. This exclusivity—available under the Drug Price Competition and Patent Restoration Act of 1984 or better known as the Hatch-Waxman Act—can bring immense profits to the company. Dr. Reddy's, the first Indian company to get the 180-day exclusivity for marketing fluoxetine 40mg in August 2001, saw its sales of generics increasing from ₹ 304 million in 2000-01 to ₹ 4,066 million in 2001-02. Sales of fluoxetine 40 mg contributed 81 per cent of total generic sales and about half of Dr Reddy's operating profit in 2001-02 (Chaudhuri, 2007). Patent litigation under para IV is highly risky also as a failure means a loss of several years of hard work and huge legal expenses. Companies also engage in developing non-infringing processes for ANDA filing. Matrix Laboratories was the first Indian company to develop a non-infringing process for manufacturing citalopram. The company was able to reap huge benefits; its sales of the product were ₹ 5,600 million till 2005-06. Another example of commercial success is the cefotaxime process developed by Lupin (Chaudhuri, 2007).

Since 2002, both Ranbaxy and Dr Reddy's have taken steps towards registering themselves as the first movers for a number of generic drugs. Data obtained from the FDA show that while Ranbaxy has been able to obtain approvals for 22 drugs as 'first-time generics' between 2002 and 2005, Dr Reddy's has been able to obtain similar approvals for eight drugs (Dhar and Gopakumar, 2006). More recently, Glenmark got first-to-file status for three drugs having a combined revenue of over $2 billion. The three drugs are Zetia (ezetimibe) with annual sales of $1.5 billion in the US in 2008, Tarka (trandolapril+verapamil) with annual sales of $72

million and Cultivate (fluticasone lotion) with annual sales of $37 million.[13]

Only a few companies, such as Ranbaxy and Dr Reddy's, had ANDAs in their name till recently. Companies such as Cipla had ANDAs in the names of their marketing partners in the US. This situation has changed dramatically in recent times and more companies are engaged in securing ANDAs. From 161 ANDAs filed by four companies—Ranbaxy, Dr Reddy's, Wockhardt and Lupin—in the last quarter of 2003, the number has gone up to 701 ANDAs filed by 17 companies by the second quarter of 2007 (Chaudhuri, 2007). ANDA approvals held by Indian firms as a percentage of total approvals have gone up sharply from 7 per cent in 2001 to 21 per cent in 2006, 30 per cent in 2008 and 35 per cent in 2009 (till 23 February).[14]

A significant recent development for the Indian firms is their entry in the market for anti-retroviral (ARV) drugs in the US. Two firms, Ranbaxy and Aurobindo Pharma, were able to obtain tentative or full approval from the US Department of Health and Human Services and the FDA for five ARV drugs during 2004-05. These drugs were approved as part of the President's Emergency Plan for AIDS Relief (PEPFAR) that President George W. Bush had announced in 2003 for bringing low-cost, high-quality ARV therapy to patients. The Indian firms had also marked their significant presence in the implementation of the Global Fund to Fight AIDS, Tuberculosis and Malaria that was established in 2002 (Dhar and Gopakumar, 2006).

Major Indian firms such as Ranbaxy, Dr. Reddy's, Sun Pharma and Cipla are certified suppliers of generic medicines in the European Union (EU), in particular the UK. Dhar and Gopakumar (2006) point out that Ranbaxy and Dr. Reddy's have led the way and they have been joined by Aurobindo Pharma, Primal and Orchid Healthcare. Ranbaxy obtained the largest number of approvals

13. These drugs are manufactured by Schering-Plough, Abbot and Sanofi Aventis and Nycomed respectively. For details, see "Glenmark gets First to file Status for Three Drugs",*The Times of India*, July 3, 2009.

14. See Chaudhuri (2007) and "USFDA Door wide open for Indian Pharma Cos", *Business Standard*, March 6, 2009.

(204), followed by Dr. Reddy's (57). Although Indian interest is expanding in the EU, it is generally viewed as problematic compared to the US due to barriers such as different regulatory approval requirements within the community, linguistic difficulties and complex pricing dynamics (Sampath, 2008).

Table 4.6

Share of Exports of Intermediates and Bulk Drugs: Region-wise

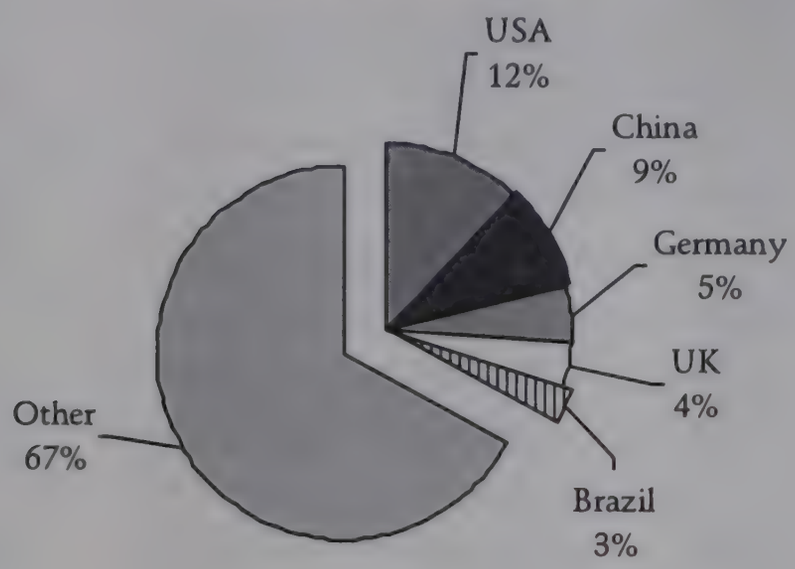
	Africa	*US*	*Asia*	*Europe*
1994-95	5	15	38	42
1995-96	6	17	41	36
1996-97	5	18	43	32
1997-98	6	20	41	32
1998-99	8	22	44	26
1999-2000	8	20	43	28
2000-01	7	23	42	27
2001-02	6	26	40	26
2002-03	7	29	37	26
2003-04	7	27	35	30
2004-05	7	28	35	29
2005-06	9	20	41	30
2006-07	11	23	36	29
2007-08	12	22	37	28

Source: DGCIS.

The trends in exports of intermediates and bulk drugs are quite different. Table 4.6 shows that there is a shift in the focus of exports from Europe to other regions. The share of exports to Europe has declined from 42 per cent in 1994-95 to 28 per cent in 2007-08. Asia has now become the leading export destination, accounting for more than a third of total intermediate and bulk drug exports. The combined share of Africa and the Americas has increased from 17 per cent in 1990-91 to 34 per cent in 2007-08. China, Singapore and Thailand account for 40 per cent of exports to Asia. The US accounts for more than half (54.5%) of the exports to the Americas, followed by Brazil and Mexico. These three countries together account for 79 per cent of the exports to the Americas.

Figure 4.3

Top Five Destination Countries in the Export of Intermediates and Bulk Drugs, 2007-08



Source: DGCIS.

The US is the single largest destination of exports of intermediates and bulk drugs, accounting for 12 per cent of exports, followed by China, Germany, the UK and Brazil. These five countries account for 33 per cent of total exports of intermediates and bulk drugs (Figure 4.3).

Can the strong showing of the pharmaceutical industry in India, in particular the generics sector, which has provided much-needed depth to the industry, be sustained over a period of time? This question can best be answered by analysing the performance of the generics sector in the realm of technology. The following discussion provides the details in this regard.

The Indian Generics Industry and Access to HIV/AIDS Drugs

Universal access to drugs is a well-recognised strategy to counter the spread of HIV/AIDS. In 1996, Brazil took a bold decision to pave the way for free ARV treatment. Even though Brazil started the free ARV treatment programme using drugs from the brand-name firms, the high cost of patented ARV drugs saw it later shift to generic drugs to ensure the sustainability of the programme. Till 2000, the cost of ARV drugs was between $10,000 and $15,000 per person per

year (ppy). As a result, free treatment programmes were beyond the reach of most countries. The high cost of patented ARV drugs forced the Brazilian government to start domestic production of these drugs. Thus Brazil introduced the first generic version of ARV drugs, which was priced at $3,000 ppy. This showed for the first time that ARV drugs can be produced at a lower price than that of the patented drugs, and it accelerated the demand for cuts in ARV drug prices.

The Indian firm Cipla took an initiative to reduce the prices of ARV drugs, which triggered a 'domino effect.' In February 2001, Cipla announced that it would sell a triple ARV combination[15] for $350 ppy. This shattered many myths about drug prices. The announcement forced brand-name firms to cut their prices. The fall in the prices of ARV drugs encouraged many governments and non-governmental organisations (NGOs) to initiate free ARV treatment programmes. Generics thus became the focal point of all free ARV treatment programmes including the US' PEPFAR. Presently, a first-line triple combination is available at $132 ppy.

Indian generics firms have made three path-breaking contributions to the availability and accessibility of ARV drugs. Firstly, they started producing and marketing the generic versions of first-line triple combination drugs at an affordable price. This triggered a price war in the ARV drug segment. Secondly, Indian firms introduced fixed dose combinations (FDCs) of ARV drugs. As a result, the number of pills was reduced from six pills per day to two per day. FDCs not only improved the adherence but also reduced the price of ARV drugs. Thirdly, Indian firms also introduced the paediatric formulation of ARV drugs.

Producers of ARV drugs in India benefited from the fact that the Indian Patents Act did not allow patenting of pharmaceutical products until the Act was amended in 2005.

Following Cipla's lead, other generics firms also entered the ARV drug segment. Currently 14 firms are active in ARV drug production (Table 4.7). Out of these, eight firms are active only in the active pharmaceutical ingredient (API) segment of ARV production.

15. Cipla's triple combination comprised stavudine, lamivudine and nevirapine.

Table 4.7

Firms Active in ARV Drug Production

Firm	*API*	*Formulation*
Cipla Ltd.	√	√
Ranbaxy Laboratories Ltd.	√	√
Aurobindo Pharma Ltd.	√	√
Strides Arcolab Ltd.	√	√
Hetero Drugs Ltd.	√	√
Emcure	√	√
Zydus Cadila Healthcare Ltd.	√	
Sun Pharmaceutical Inds. Ltd.	√	
Samarth Pharma Ltd.	√	
Matrix Laboratories Ltd.	√	
IPCA Laboratories Ltd.	√	
Dr. Reddy's Laboratories Ltd.	√	
Eastern Surgical Company	√	
Macleods	√	

Source: *Annual reports* of firms (various years).

Possibly the most significant dimension of the operations of the Indian firms in the market for ARV drugs is that they have emerged as a major source of supply to the affected countries. Seven firms have obtained registrations for supplying ARV drugs as of October 2005, the details of which are provided in Table 4.8.

Table 4.8

Approvals Received by Indian Firms for Supplying ARV Drugs

Firm	*Total Drugs Registered*	*WHO Pre-qualified Drugs*
Aurobindo Pharma Ltd.	41	3
Cipla Ltd.	31	10
Eastern Surgical Company	22	...
Emcure Pharmaceuticals Ltd.	16	...
Hetero Drugs Ltd.	23	1
Ranbaxy Laboratories Ltd.	21	7
Strides Arcolab Ltd.	11	4

Source: WHO, Regulatory Status of Antiretroviral Drugs Database (last update on October 25, 2005).

The largest number of registrations has been granted to Aurobindo Pharma, although it is Cipla which has the largest number of WHO pre-qualified drugs. The other noteworthy feature of the registrations granted to the Indian firms is that all the firms, with the exception of Eastern Surgical and Emcure, have registered their presence in most countries of Africa, which is by far the most affected region.

The Indian firms have also proved their capabilities in terms of supplying the ARV drugs to the affected countries. Since the Global Fund to Fight AIDS, Tuberculosis and Malaria started providing funds for the free treatment programme, Indian firms have emerged as major suppliers of ARV drugs. Between June 2003 and January 2006, more than 1,300 consignments of ARV drugs were supplied under the Global Fund, and of these Cipla is the largest supplier.[16] Table 4.9 gives the list of top 10 suppliers of ARV drugs under the Global Fund.

Table 4.9

Top 10 Suppliers of ARV Drugs under the Global Fund in Terms of Consignments (June 2003 to January 2006)

Firm	*No. of Consignments*
Cipla Ltd.*	342
Aspen Pharmacare*	221
Bristol Myers Squibb	158
GlaxoSmithKline Ltd.	144
Abbott Laboratories	88
Merck	73
Ranbaxy Laboratories Ltd.*	45
Hetero Drugs Ltd.*	35
Roche	32
Boehringer Ingelheim	25

Note: * Supplied from a single source.

Source: Global Fund to Fight AIDS, Tuberculosis and Malaria (*www.theglobalfund.org/en/about/procurement/list/*).

Although three Indian firms were among the top 10 suppliers of ARV drugs under the Global Fund in terms of the number of

16. A part of Cipla's supplies was met by its marketing joint venture in South Africa, Cipla Medpro.

consignments, only two figured among the top nine suppliers in terms of value of drugs supplied. Table 4.10 provides the details.

Table 4.10

Top Nine Suppliers of ARV Drugs under the Global Fund in Terms of Value (June 2003 to January 2006)

Firm	*Total Value ($ million)*
Bristol Myers Squibb	8.0
Cipla Ltd.	7.4
GlaxoSmithKline Ltd.	3.9
Roche	3.5
Merck	3.1
Aspen Pharmacare	3.1
Abbott Laboratories	0.8
Ranbaxy Laboratories Ltd.	0.7
Boehringer Ingelheim	0.6

Source: Global Fund to Fight AIDS, Tuberculosis and Malaria (*www.theglobalfund.org/en/about/procurement/list/*)

Between June 2003 and January 2006, the Global Fund provided nearly $34 million for procuring ARV drugs; the share of the Indian firms was close to 25 per cent. This establishes the point that Indian firms have become major global suppliers of ARV drugs, particularly in recent years. The future of the generics firms therefore becomes important in relation not only to India's quest to obtain drugs at affordable prices, but also to its pivotal position as a supplier of ARV drugs to some of the most affected regions in the world. The following section looks at the future of India's ARV drug production capacity under the product patent regime.

Product Patents and the Future of Generic ARV Drugs

The introduction of a product patent regime in India has created serious doubts on the future supply of generic ARV drugs. The availability of generic ARV drugs is required to meet both the domestic and export markets. Further, countries worst affected by HIV/AIDS do not possess the technical expertise to produce ARV drugs. These countries have to depend on countries like India, Brazil

and China[17] for the supply of generic ARV drugs, even in the absence of product patent protection at the domestic level. In other words, access to drugs in many countries depends upon the flexibility available in the patent laws of major generic-producing countries.

The introduction of product patenting in India raises several concerns. These include:

(i) Whether the product patent regime would affect the supply of generic ARV drugs from India?

(ii) Whether Indian firms can produce ARV drugs that are currently available but are not produced in India?

(iii) Whether India can export ARV drugs to countries having no or insufficient manufacturing capacity in the pharmaceutical sector?[18]

(iv) How Indian firms will produce new ARV drugs in the pipeline?

Future of Existing Supply

All currently available ARV drugs were invented and patented in the US or other developed countries before 1995. Hence, these drugs *per se* are not eligible for patent protection in India because the WTO's agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS) requires India to consider grant of product patents only for drugs that were invented after January 1, 1995. In other words, India would have to recognise only the post 1995 patents, that too if the applications are submitted in the country. It may, however, be argued that the latter patents would be in the nature of improved formulations which are not eligible for patenting in India, following the provisions of Section 3(d) of the Indian Patents Act as amended. According to this section, the following is not considered an invention: "the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new

17. It may be pointed out that China's existing strength is in production of APIs and not formulations.

18. As provided in the WTO's Doha Declaration on the TRIPS Agreement and Public Health. See WTO (2001a) for details.

property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant."[19]

This section, however, qualifies the exclusion with efficacy requirements. As a result, if the applicant proves that the claimed invention increases the efficacy of the known substance, a patent can be granted. In this context, it needs to be pointed out that the Indian Patent Office is not yet well equipped to evaluate claims on efficacy, and that patent applicants may eventually get a favourable nod from the authorities. Further, patents are filed before the marketing approval of drugs; therefore, it is not possible to make a claim on efficacy at the time of filing. Pharmaceutical firms could use this exception to claim patents on a known substance in order to extend the patent monopoly. For instance, in the patent dispute over the cancer drug Gleevec, it was observed that the patent applicant Novartis relied on the efficacy argument to defend its claim on a beta-crystal format of a known substance invented in 1993. The Indian patent authority accepted the efficacy argument but rejected Novartis' claim on lack of evidence in this regard.

In India, several firms have filed patent applications claiming that their inventions constitute improvements of known substances. Table 4.11 provides a non-exhaustive list of pending patent applications on ARV drugs in the 'mailbox.' These applications have claimed patents either in the salt form or in the form of combinations or isomers. Therefore, patents on any of these claims may affect the availability of existing ARV drugs. Even though the Indian Patents Act provides immunity to the existing producers of ARV drugs, patents on such drugs would increase the cost of these drugs since payment of royalties to the patent holder is entailed. The patent holder could try to extract supernormal rents by way of royalty payments, given that the language of Article 11A of the Patents Act, which operationalises the 'immunity provision,' allows such possibilities. These supernormal rents could be reflected in

19. The explanation accompanying this section provides further clarification as regards the scope: "For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy."

the price of generics. Further, in the absence of a clear ceiling on royalties, the patent holder may raise the royalty rate. This may lead to a situation where patients on existing ARV treatment may end up paying an increased price.

Table 4.11

Pending Product Patent Applications for ARV Drugs Filed in India

Substance	*Title*	*Indian Application No.*	*Priority Date*	*Applicant*
Lamivudine + zidovudine	Pharmaceutical compositions	2044/CAL/1997A	31/10/1996UK	Glaxo
Nevirapine/ hemihydrate	Pharmaceutical suspension comprising nevirapine hemihydrate	2485/DEL/1998A	NA	Boehringer Ingelheim
Trizivir	Anti-viral combinations	1206/CAL/1997A	NA	Glaxo
Tenofovir-3 applications	Nucleotide analog composition	986/DEL/2002A	25/7/97/US	Gilead
	Nucleotide analog composition	963/DEL/2002A	25/7 /97/US	Gilead
	A method for preparing Form 2 or Form 4 crystalline adefovir dipivoxil	989/DEL/2002A	25/7 /97/US	Gilead
Lamivudine	Pharmaceutical compositions	479/CAL/1998A	24/03/1997& 26/03/1997	Glaxo
Amprenavir + AZT + Ziagen	Anti-viral combinations	1206/CAL/1997A		Glaxo
Amprenavir+ AZT+3TC+ FTC	Vaccine	2172/MAS1998A	26/09/1997	SmithKline Beecham
Amprenavir	Pharmaceutical formulations	727/DEL/1997A	22/03/1996USA	Glaxo
Abacavir	A novel salt	872/CAL/98	17/5/97UK	Glaxo
Lexiva fosamprenavir calcium	Calcium (3S)	IN/PCT/2001/00039	18/7/1998 GB	Glaxo
Lopinavir	Process and intermediates for preparing retroviral protease inhibitors	259/MUMNP//2003	31/08/2000	Abbott

Source: Government of India, Controller General of Patents Designs and Trademarks (*www.patentoffice.nic.in/*)

Production of Existing ARVs

As stated earlier, the introduction of generics has brought down the prices of first-line ARV drugs. However, patients who are already on first-line drugs will need to change to the second-line treatment, which is very costly. For instance, until recently, Brazil spent 63 per cent of its ARV drug budget on only three second-line ARV drugs.

Table 4.12 shows the comparative price difference between first-line and second-line drugs. It shows that the price of second-line drugs is exorbitant and people who develop resistance to the first-line drugs may not be able to afford switching over to the second line. The high cost could also raise serious questions on the sustainability of free treatment programmes initiated by countries. It hardly needs to be emphasised that this issue should be addressed to avoid a public health catastrophe.

Table 4.12

Price Comparisons of First- and Second-Line ARV Regimens

Country	*First-line Regimen*	*Price in $ (ppy)*	*Second-line Regimen*	*Price in $ (ppy)*
Cameroon	3TC/d4T/NVP	277	AZT+ddi+NFV	4,763
Malawi	3TC/d4T/NVP	288	AZT+ddi+NFV	1,875
Kenya	3TC/d4T/NVP	292	AZT+ddi+NFV	1,594
Cambodia	3TC/d4T/NVP	350	AZT+ddi+LPV/r	1,215
Thailand	3TC/d4T/NVP	352	AZT+ddi+SQV/r	3,500
Honduras	3TC/d4T/NVP	426	D4T+ddi+NFVor AZT+ddi+NFV	3,796 (NFV only)

Source: Medecins Sans Frontieres (2005).

Table 4.13 shows that Indian firms are producing 13 out of 20 ARV drugs which are currently available for treatment. Most of these drugs were in production prior to 2005 and therefore eligible for the immunity clause under Section 11A of the Patents Act as amended. However, the immunity clause would not apply to drugs which were not produced prior to 2005. Seven ARV drugs are outside the scope of the immunity clause. Currently, Indian firms are producing seven types of FDCs which are used for first-line treatment (Table 4.14). But FDCs required for second-line

treatment are not eligible for immunity. Likewise, emtricitabine, tenofovir and saquinavir have only one producer. Hence, Indian firms cannot start producing and marketing these drugs if patents are granted. Therefore, the future of the mailbox applications would determine the accessibility of these drugs. As Table 4.11 shows, a number of patent applications on lopinavir and amprenavir, including those that are in the mailbox, are awaiting examination. Further, production of FDCs also would be affected if patents on the combinations were granted. Table 4.14 shows that at least one such combination, which may be useful in the future, has its patent application pending in the mailbox. Hence, application of Section 3(d) of the Patents Act would determine the availability of those seven drugs and the FDCs for second-line drugs.

Table 4.13

Existing ARV Drug Production Capacities of Indian Firms

Drug	*Cipla*	*Ranbaxy*	*Aurobindo*	*Strides*	*Hetero*	*Emcure*
Nucleoside reverse transcriptase inhibitors (NRTIs)						
Abacavir	√	√			√	
Didanosine (ddI)	√	√			√	
Lamivudine	√	√	√	√	√	√
Stavudine (d4T)	√	√	√	√	√	√
Zalcitabine (ddC)						
Zidovudine (AZT)	√	√	√	√	√	√
Emtricitabine (FTC)					√	
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)						
Delavirdine						
Nevirapine	√	√	√	√	√	√
Tenofovir					√	
Efavirenz	√	√	√	√	√	√
Protease inhibitors						
Amprenavir						
Indinavir	√	√		√		
Nelfinavir	√			√	√	
Ritonavir	√			√	√	
Saquinavir				√		
Lopinavir + ritonavir						
Atazanavir						
Fosamprenavir calcium						
Fusion inhibitors						
Enfuvirtide						

Source: *Annual reports* of the firms.

Table 4.14

Production of Fixed Dose Combinations by Indian Firms

Combination	*Aurobindo*	*Cipla*	*Ranbaxy*	*Strides*	*Hetero*	*Emcure*
Lamivudine + stavudine + nevirapine		√	√	√	√	√
Lamivudine + zidovudine + nevirapine		√	√		√	√
Abacavir + lamivudine + zidovudine			√		√	
Lamivudine + stavudine		√		√	√	√
Lamivudine + zidovudine	√	√		√	√	√
Lopinavir + ritonavir					√	
Emtricitabine + tenofovir					√	

Source: *Annual reports* of the firms.

This brings the focus onto the compulsory licensing regime in India. To follow the above strategy, there is a need for a simple and easy-to-use compulsory licensing regime. However, the present regime is not very useful in this regard. Generally, a compulsory licence is available only three years after the date of grant of the patent. The only exception is for a situation of national emergency, extreme urgency or public non-commercial use. Even though HIV/AIDS is in effect a national emergency for India, the government has not officially recognised it as such.

Concluding Remarks

The Indian pharmaceutical industry has witnessed considerable changes over the past few decades, particularly with the emergence of a strong generics industry. The growth of the industry and its subsequent consolidation was largely contributed by the Patents Act that was enacted in 1970. The Patents Act, 1970, had two key features that facilitated the growth of the generics industry in India. Firstly, only process patents were allowed for chemical entities, including pharmaceuticals, and secondly, the term of protection was made shorter for pharmaceutical patents. The process patent regime enabled the generics firms to develop alternative processes for manufacturing products that were already in the market. Although critics claimed that the reverse-engineering that the generics firms

were engaged in was tantamount to counterfeiting, none of the generics manufacturers could be challenged by the global firms whose products they were reverse-engineering.

The patents regime that the Patents Act, 1970, introduced underwent a change following implementation of the commitments India had assumed under the TRIPS Agreement of the WTO. The TRIPS-consistent patent regime brought with it uncertainties for the generics manufacturers, for their ability to reverse-engineer products would be limited to a considerable extent. Furthermore, India is under pressure to introduce data exclusivity (see below), a move that could also affect the future prospects of the generics manufacturers.

This study analysed the performance of the Indian pharmaceutical industry in the post-TRIPS patent regime. The analysis covered the period post-1995 when India acceded to the WTO. Our analysis showed that the leading generics firms in the industry have displayed considerable dynamism since 1995. The consolidation of the Indian firms, which began in the first half of the 1990s, improved considerably since the beginning of the current decade. Particularly noteworthy was the increase in the R&D spending of some of the leading firms, in particular, Ranbaxy and Dr. Reddy's. As a result, R&D intensities of the firms have improved significantly.

The R&D efforts of the leading generics firms have borne considerable fruit. Market approvals in the US and the UK, in particular, have increased in the past few years. Both Ranbaxy and Dr. Reddy's have developed improved generics and Novel Drug Delivery Systems (NDDS), which have opened the door for collaboration with the pioneer producers. India is fast emerging as the hub for contract research and manufacturing, with a number of pharmaceutical majors establishing joint ventures with the Indian generics producers.

Although Indian firms are yet to make a mark in new drug discoveries, they are on course for major developments even on this front, given the sharp increase in their patenting activity of late. This activity could be strengthened by the increased efforts made

by the government to participate in the R&D activities involving the industry.

These efforts to strengthen the technological sinews of the Indian generics industry should stand the industry in good stead as it evolves strategies to meet the challenges posed by the post-TRIPS patent regime. Improvements in the generic versions of proprietary drugs have become the established strength of the generics industry in India, and with the prospects of faster growth of the market for generics in the near future, the industry should be looking at major gains.

One area where the Indian industry has got its act in place is the market for ARV drugs. Supplying these drugs at prices that the population of the affected regions can afford has become a priority and several of the Indian firms have met considerable success. With the global community now focused on obtaining drugs at affordable prices, it appears increasingly probable that the pharmaceutical industries in the developing world, like the one existing in India, would offer the much-needed solutions.

These successful forays of the generics firms would have to be assessed in the context of its role in securing access to medicines at affordable prices. We have indicated that the penchant for patenting, involving incrementally modified drugs at that, does draw attention to the bleak side of the industry. Besides, R&D priorities are increasingly being set in tune with the global trends, and this focus has increased since the firms have enhanced their level of collaboration with foreign firms. Particularly affected in this process would be the 'neglected diseases.'

The above-mentioned concerns arising from the successes of the Indian pharmaceutical industry have important policy lessons for developing countries. In the first instance, it is necessary to provide sufficient flexibilities in patent laws so that the domestic pharmaceutical industries can get a chance to develop. It must be recognised, however, that the advantages that the Indian policymakers could provide to their nascent pharmaceutical industry in the 1970s, by way of introducing a process patent regime, cannot be replicated in a TRIPS-determined patent system. Nevertheless,

developing countries can provide an enabling environment for their domestic industries by carefully designing provisions that relate to patentable subject matter and compulsory licences.

It is also important to examine the implications of introducing a data exclusivity regime in India while implementing Article 39.3 of the TRIPS Agreement. This Article requires WTO member countries to provide protection to test and other data when such data are submitted to the regulatory authorities in the process of obtaining marketing approval for a pharmaceutical product.

A data exclusivity regime would have quite considerable ramifications for the Indian generics industry. Introduction of a data exclusivity regime of the kind prevailing in the US and the EU would be a death knell for the generics firms in India. The consequences of this threat faced by generics industries would be felt by most sections of the populations not only in the countries that are home to these industries but also in other countries which have been dependent on the industries.

It is important to point out that the position taken by industry associations of the pharmaceutical majors, which has been endorsed by the US trade administration through its annual Special 301 reports, is a violation of the multilateral system. Neither Article 39.3 of the TRIPS Agreement nor Article 10 bis of the Paris Convention requires that WTO member countries introduce data exclusivity regimes of the kind that the US and the EU provide. The attempts to impose global standards of data exclusivity are aimed at ensuring that the pharmaceutical majors get protection for their products in perpetuity, thus maintaining their stranglehold over the pharmaceutical market.

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5

K.M. GOPAKUMAR

Patent and Access to Medicine

Constraints for the Use of Flexibilities

Introduction

In order to comply with the agreement on the Trade-Related Aspects of Intellectual Property Rights (TRIPS), India introduced product patent protection from January 1, 2005. In doing so, India used 10 years transition period available under the TRIPS and delayed the introduction of product patent protection to pharmaceutical inventions. While meeting the TRIPS obligation, Indian policy makers were confronted with two major concerns, *viz.*, the future of the Indian pharmaceutical industry, and access to affordable medicines within the country and other developing countries. Thus the "major concern was how the adoption of intellectual property regimes would affect their efforts to improve public health, and economic and technological development more generally, particularly if the effect of introducing patent protection was to increase the price and decrease the choice of sources of pharmaceuticals" [Commission on Intellectual Property Rights (CIPR), 2003: 29].

To make use of the flexibilities available within and outside of TRIPS turned out to be the most pragmatic solution before the developing countries including India to address the concerns on the availability and accessibility of medicines. According to this approach, TRIPS provides only minimum standards of protection and does not set the universal common standard for the substantial aspects of the patent law. This strategy obtained the political consensus at the Doha Ministerial Conference of 2001.

The Conference adopted a separate declaration, *viz.*, the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration), which clearly states "the right of WTO members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose."[1] Thus the TRIPS implementation strategy was "to find the means within the patent system and outside it, to generate the competitive environment that will help to offset the adverse price effect of patents on developing country consumers. The cautious approach suggests the implementation of TRIPS should be done with minimum damage" (CIPR, 2003: 38).

Thus for India, the incorporation of TRIPS flexibilities (public interest safeguards) in the domestic legislation is the dominant strategy for balancing the public and private interests, while implementing the TRIPS compliant patent regime. However, the success of the TRIPS flexibilities in addressing the question of access to affordable medicines mainly depends on three factors: (i) the incorporation of flexibilities in the domestic law; (ii) the manufacturing capability of a country; and (iii) the political will to use the public interest safeguards provided in the domestic law.[2]

In India, the policy prescription for the implementation of the TRIPS flexibilities accepted the strategy of their incorporation in the domestic law. However, there was no consensus among the various actors regarding the scope of the flexibilities to be made available in the Indian Patents Act 1970, while implementing the TRIPS patent regime. The implementation of the TRIPS flexibilities involves changes far beyond an amendment of the law and it required policy and institutional support for the implementation of flexibilities. This article identifies and examines the legal, policy and institutional challenges that India is currently facing in

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1. Paragraph 4, Doha Declaration on the TRIPS Agreement and Public Health.

2. The question of access to affordable medicine is not merely an issue related to the availability of affordable medicines, but also linked to the developing countries' industrial and economic development. Hence, the author recognises the need to look at the implications of TRIPS on the policy space for industrial and economic development of the developing countries. However, this article does not directly focuses on the issue of implications of TRIPS on industrial and economic policy space for developing countries, rather it focuses on the policy space for the Indian generic pharmaceutical industry to produce new medicines at affordable price.

the implementation of the TRIPS flexibilities. In other words, it examines the utility of the TRIPS flexibilities in the Indian context.

The second section analyses the changes in India's patent law and examines the implementation of the TRIPS flexibilities brought in with these changes. Further, it also identifies the policy and institutional bottlenecks in the implementation of the TRIPS flexibilities in the country. The third section provides the conclusion and general recommendations of the study.

Implementation of TRIPS Flexibilities

India has carried out three amendments to fully comply with TRIPS patent regime. The primary aim of these amendments is to fulfil the TRIPS obligations, along with the incorporation of the TRIPS flexibilities in the domestic legislation. However, the amendments are also used to increase the efficiency of patent administration. In order to comply with the TRIPS obligation, India amended the Patents Act in 1999 (to introduce Exclusive Marketing Rights (EMR), 2002 (to comply with rest of the obligations except product patent) and 2005 (to introduce product patent regime). A critical examination of relevant provisions of Patents Act is carried out below to find out how far the Indian Patents Act (Act) has incorporated TRIPS flexibilities.

Scope of Patentability

One of the important concerns related to the introduction of product patent protection is the patenting of known substances. Often pharmaceutical companies misuse the patent protection to seek patents on known substances claiming incremental modifications as inventions. This practice is known as 'evergreening of patents.'[3] Such practice is aimed to delay the generic competition by acquiring as many patents on the known substance. Therefore, a strict patentability criterion, which denies patent protection to known substance, is essential to ensure early entry of generic medicines.

3. For a detail discussion on the patenting strategies of pharmaceutical MNCs, see Abbrol (2004).

Generally speaking, there are two ways to limit the scope of patentability. First, increase the threshold limit of patentability criteria by providing the definition of patentability criteria, *viz.*, novelty, inventive step and industrial applications. Second, to exclude certain types of inventions, which do not satisfy any one of the patentability criteria, or those inventions which are in conflict with public morality, national security or affecting the health of humans, animals and plants. The Indian Patents Act attempts to limit the scope of patentability by following both methods. The criteria for patentability are defined in the Act and linked to a web of definitions. According to the Act, a patent means "a patent for any invention granted under this Act."[4] The word 'invention' is defined as a "new product or process involving an inventive step and capable of industrial application."[5] Thus a patent is granted only to a new product or process involving an inventive step and capable of industrial application. However, the Act defines 'inventive step' as "a feature of an invention that involves technical advances as compared to the existing knowledge or having economic significance or both and that makes an invention not obvious to a person skilled in the art."[6] According to this definition, to qualify the inventive step test, the invention has to satisfy any of the three conditions, *viz.*, advances over existing technical knowledge or economic significance or both. Generally speaking, economic significance should not be a sole criterion for evaluating the inventive step of the invention. The economic significance of an invention depends on many other factors and it is not the purpose of patents to recognise economic significance of an invention. However, the new definition makes the economic significance criteria as substitutable criteria to technical effect. As a result, the new definition of inventive step diluted one of the basic requirements of an inventive step. TRIPS uses economic significance in a different context. Under Article 31(l)(ii), TRIPS states that compulsory licence for dependent patent should look at whether the second patent should involve an important technical advancement of considerable economic significance in relation to

4. Section 2 (m) of Patents Act.
5. Section 2(j) of Patents Act.
6. Section 2(ja) of Patents Act.

the invention claimed. Therefore, economic significance could have been used along with the technical effect to judge the inventive step, but not as the sole criteria. Therefore, the current definition lowers the threshold level for the inventive step. The third amendment also introduced two more definitions, with an objective of limiting the scope of patent protection.[7]

Section 3 of the Patents Act excludes 16 categories of inventions from patent protection, because they are not considered inventions within the definition of invention. There are a few exclusions having implications to the patentability of pharmaceutical substance.[8] However, the most important exclusion is in sub-section (d), which states:

> The mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new

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7. The Act included two new definitions, *viz.*, new invention and pharmaceutical substance with the intention of limiting the scope of patentability. New invention means any invention or technology, which has not anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, i.e., the subject matter has not fallen in public domain or that it does not form part of the state of the art. Hence, to qualify as a new invention, the invention in question should not have been either published in any document or used in India or anywhere in the world before the filing of patent with complete specification. It means the subject matter has not fallen either in public domain or became part of the state of art. The notable omission here is the publication does not include oral publication. As a result, it fails to recognise oral knowledge as an element in the definition. Further, this definition makes a difference between invention and technology. The common understanding is that invention in the patent context is related to the technology and therefore this differentiation does not make any sense. Hence, it does not serve any purpose. The meaning of definition reflects that it is intended to define the word 'new.' Likewise, the definition of pharmaceutical substance is not linked to the patentability of pharmaceuticals. According to the definition, the term 'pharmaceutical substance' "means any new entity involving one or more inventive step." Thus the definition expanded the scope of pharmaceutical substance and encompasses every type of pharmaceutical entity including, but not limited to, formulations, pharmaceutical salts, isomers, polymorphs and their combinations. Nevertheless, both definitions have not been linked to other provisions of the Act. Therefore, these definitions are stand-alone and provide some kind of incoherence to the statute. If it is used to interpret the patentability criteria, these definitions would dilute the threshold levels of patentability criteria.

8. Section 3 (a): An invention which is frivolous or which claims obviously contrary to well-established natural laws.

   Section 3(e): A substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance.

   Section 3(p): An invention which, in effect, is traditional knowledge or which is an aggregation or duplication of known properties of traditionally known component or components.

> reactant. For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations, and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy.

This provision excludes new forms of known substance, discovery of new property of known substance and new use of known substance. Further, it treats salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance as the same substance. Therefore, subsequent patenting in any of the above-mentioned forms is prohibited.

However, the exclusions in sub-section (d) do not prohibit patenting of known substances in all circumstances. Exclusions are qualified with word 'mere' and the phrase "which does not result in the enhancement of the known efficacy." These are ambiguous, too broad and potentially allow new forms of existing substances to be patented. For instance, as per the qualification, what is banned is the patenting of mere discovery of new form of known substance and the patenting of discovery of new forms of known substance *per se* is still possible. Further, a minor amendment to an existing one can satisfy the requirement of 'enhancement of efficacy,' and one is able to get around the provision as it stands. In addition, the phrase 'mere discovery' conveys that discoveries are patentable if they are not mere discoveries.[9] The mandate under TRIPS is to provide patent protection to only inventions and discoveries.

These qualifications offer an entry point in favour of the patentee to claim patents on all those types of claims mentioned in the explanation to Section 3(d). Furthermore, the patent office is not equipped like a science lab to examine whether the claimed invention differs "significantly in properties with regard to efficacy."[10] These flaws result in the expanded scope of patentability. Therefore, the current provisions of the Patents Act

9. Also see Gopakumar and Amin (2005).
10. Ibid.

do not rule out the possibility of evergreening of patents. The empirical evidence suggests that patent office failed in conducting a strict scrutiny of patent applications and granted patents on known substance, which often violates Section 3(d) (James, 2010). Provisions pertaining to the scope of patentability, i.e., definitions on the criteria of patentability and the exclusions of patentability provide enough space for pharmaceutical companies to come around the exclusions especially Section 3(d) and obtain patents for known substance. Reflecting the same view the Parliamentary Standing Committee on Commerce in its report in 2008 recommended that "The Government should clarify the usage of terms "significantly" and "efficacy", which form part of Section 3 (d), to clear the ambiguities involved in the interpretation of the said section" (Parliament of India, 2008).

This would delay the introduction of generic drugs in the market even after the expiry of original patent and compromises the access to medicines.

Irrespective of above-mentioned shortcomings of Section 3(d) in controlling evergreening of patents, pharmaceutical MNCs collectively and individually attack Section 3(d). In 2009, US-India Business Chamber (USIBC) released a report on Section 3(d) which alleges that "Section 3(d) potentially precludes the patenting of hundreds of incremental pharmaceutical innovations that Indian companies attempting to patent and commercialise outside India (USIBC and Coalition for Healthy India, 2009).

Earlier, in 2006, Novartis AG challenged the constitutional validity of Section 3(d) on two grounds at the High Court of Madras.[11] Firstly, it argued that Section 3(d) denies its rights under Article 27 of the TRIPS Agreement, which obligates WTO member states to provide patent protection to all fields of technology without discrimination, and therefore violates the obligations under the TRIPS Agreement. Secondly, it argued that in the absence of a definition or guideline, phrases like "enhancement of the known efficacy" or "differ significantly in properties with regard to efficacy" give uncontrolled as well as unguided powers

11. Novartis AG *versus* Union of India (W.P. 24759/06).

to the controller of patents. The same would result in the arbitrary exercise of powers and violates right to equality under Article 14 of the Constitution of India. In India, a challenge to the constitutional validity of a statute is maintainable only on two grounds, *viz.*, legislative competency and violation of the Fundamental Rights. However, during the course of the proceedings, Novartis mainly relied on the second ground.

The court refused to examine whether Section 3(d) violates the obligations under the TRIPS Agreement and held that:

> ...this court has no jurisdiction to decide the validity of the amended section, being in violation of Article 27 of TRIPS, we are not going into the question whether any individual is conferred with an enforceable right under TRIPS or not. For the same reason, we also hold that we are deciding the issue namely, whether the amended section is compatible to Article 27 of TRIPS or not.[12]

In fact, the court urged the Novartis AG (Switzerland) to approach the dispute settlement mechanism provided under the WTO framework. However, the very next day the federal councillor, Department of Economic Affairs for the Swiss Confederation, stated "we must have a reliable TRIPS system and the one in India is good enough. The Swiss government never gets involved in any judicial pronouncements of other countries."[13] This effectively ruled out the possibility of approaching WTO dispute settlement body.

On the issue of Section 3(d) being violation of right to equality owing to the arbitrariness and vagueness of the phraseology, the court held that:

> ...in sum and substance what the amended section with the explanation prescribes is the test to decide whether the discovery is an invention or not is that the patent applicant should show the discovery has resulted in the enhancement of the known efficacy of that substance and if the discovery is nothing other than the derivative of a known substance, then,

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12. Novartis AG and another v. Union of India and others, W.P. Nos. 24759 and 24760 of 2006, High Court of Madras, Date of Judgment: August 6, 2007.

13. See, "Swiss Govt. won't take Novartis Case to WTO", *Business Standard*, August 8, 2007, available at *http://www.rediff.com/money/2007/aug/08swiss.htm*, accessed on December 23, 2009.

> it must be shown that the properties in the derivatives differ significantly with regard to efficacy."[14]

The court also clarified the meaning of the term 'efficacy.' According to the court,

> ...the meaning of the word efficacy and therapeutic effect .... What the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease/having a good effect on the body?"[15]

Thus the court equated the meaning of efficacy with the therapeutic effect on the body. While doing so, the court also accepted the argument of the respondents that:

> ...Petitioner is not a novice to the pharmacology field but it, being pharmaceutical giant in the whole of the world, cannot plead that they do know what is meant by enhancement of a known efficacy and they cannot show the derivatives differ significantly in properties with regard to efficacy.[16]

Hence it was held that the patent applicant has to show enhanced therapeutic effect in order to obtain a patent for a new form of a known substance or for its derivatives. Therefore, the court held that Section 3(d) is not in violation of Article 14 of the Constitution of India.[17]

The Supreme Court of India concurred the reasoning of the High Court of Madras. The Supreme Court judgment has brought great degree of clarity with regard to the term 'efficacy.' The Supreme Court interpreted the term to include only therapeutic efficacy in line with the interpretation of the Madras High Court. The Supreme Court rejected any efficacy claim with regard to the physical property without any corresponding enhancement in therapeutic efficacy.

The Supreme Court clearly held that "What is evident, therefore, is that not all advantageous or beneficial properties are relevant, but

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14. Ibid.
15. Ibid.
16. Ibid.
17. Novartis petition challenging the order of the appellate board order of rejecting its patent application on Gleevic is still pending before the Indian Supreme Court.

only such properties that directly relate to efficacy, which in case of medicine, as seen above, is its therapeutic efficacy."

Further, the court held that "Further, the explanation requires the derivative to "differ significantly in properties with regard to efficacy." What is evident, therefore, is that not all advantageous or beneficial properties are relevant, but only such properties that directly relate to efficacy, which in case of medicine, as seen above, is its therapeutic efficacy. While dealing with the explanation it must also be kept in mind that each of the different forms mentioned in the explanation have some properties inherent to that form, e.g., solubility to a salt and hygroscopicity to a polymorph. These forms, unless they differ Significantly in property with regard to efficacy, are expressly excluded from the definition of "invention." Hence, the mere change of form with properties inherent to that form would not qualify as "enhancement of efficacy" of a known substance. In other words, the explanation is meant to indicate what is not to be considered as therapeutic efficacy."

Thus, the court has narrow down the interpretational scope for the term efficacy and limited it to therapeutic efficacy. However, the court does not answer or explain what types of elements, which can fall under therapeutic efficacy. For instance, the court does not deal with the question whether the reduction in toxicity or enhanced bioavailability can be considered for therapeutic efficacy. Hence, the patent applicant may argue that these elements constitute an enhanced therapeutic efficacy. Another round litigation may clarify the constituent elements of therapeutic criteria.

Hence, the Supreme Court while narrowing down the scope of efficacy criteria does not rule out the patent protection of known substances. In a way it reassured by stating: "the beta crystalline form of Imatinib Mesylate, does not qualify the test of Section 3(d) of the Act but that is not to say that Section 3(d) bars patent protection for all incremental inventions of chemical and pharmaceutical substances." The Supreme Court decision only narrows down the scope of the word efficacy. On ground, the patent examination should be conducted on a case-to-case basis at least on claims on known substances with enhanced efficacy. This may still

put the patent office and judiciary make vulnerable for lobbying for a favourable interpretation of the therapeutic efficacy requirement. Hence there are two tasks before the patent office to effectively translate the judgment in its day-to-day work. First, the Patent Office will be required to rework its patent examination guidelines in the light of the Supreme Court judgement and prevent grant of patents on those claims where there is improvement in drugs involving physical properties without any corresponding increase in therapeutic efficacy. Second, revoke all the patents granted in the light of Supreme Court interpretation of Section 3(d).

Compulsory Licence and Government Use

Successful functioning of compulsory licence (CL) and government use regime depends mainly on two factors, *viz.*, the potential users of CL (generic industry) and the government's ability to monitor the impact of patents on access to medicines. According to the CIPR (2003: 44), "developing countries should establish workable laws and procedures to give effect to compulsory licencing and provide appropriate provisions for government use." Further, there should be straightforward, transparent and fast procedures for the issuance of CL. The implementing legislation should fully exploit the flexibilities in the TRIPS for determining the grounds for compulsory licencing, as well as for non-commercial use by the government including production for export.[18]

According to the Patents Act, any interested person can make an application for compulsory licencing on the following grounds, *viz.*, the reasonable requirements of public have not been satisfied or the patented article is not available at an affordable price to the public or the patented invention is not working in the territory of India.[19] CL is also available for dependent patents and in national emergency, extreme emergency and public non-commercial use.[20] Further, CL is available to export to those countries having no or

18. Ibid. Also see Third World Network (TWN, 2004).

19. Section 84 of the Patents Act.

20. Section 91 of the Patents Act.

insufficient manufacturing facility in the pharmaceutical sector.[21] The Act provides an exhaustive list of circumstances in which the reasonable requirements of the public has not been satisfied.[22] It also prescribes a procedure to decide the request for CL. After receiving the application, if the controller of patents is satisfied of *prima facie* reason to grant CL, the controller directs the applicant to give copies of application for compulsory licence to the patentee and any other interested person.[23] The application is then published in the patents office's official journal. Subsequently, the controller takes a decision after hearing both the parties, i.e., the applicant and the opponent. The controller has the right to set the terms and conditions of CL in the order, and the order of the CL will operate as a deed between the parties.[24]

The Patents Act does not use all-possible grounds for granting CL. It limits the scope of refusal to grant a licence as a ground for CL. On this ground, the applicant has to prove any of the following. First, refusal to provide a licence prejudice of an existing trade or industry or the development thereof or the establishment of any new trade or industry in India. Second, the trade or industry of any person or class of persons trading or manufacturing in India is prejudiced or the demand for the patented article has not been met to an adequate extent or reasonable terms. Third, a market for export of the patented article manufactured in India is not being supplied or developed, and the establishment or development of commercial activities in India is prejudiced.[25] As a result, it refuses to provide a licence for commercial purpose.

As per the existing provisions, the applications for CL can be obtained only after three years from the date of grant of the patent.[26] The only exemption is provided in national emergency, extreme urgency and non-public commercial use. A three-year cooling period is required under the Paris Convention only when

21. Section 92(a) of the Patents Act.
22. Section 87 of the Patents Act.
23. Ibid.
24. Section 93 of the Patents Act.
25. Section 84(7) (a) of the Patents Act.
26. Section 84(1) of the Patents Act.

a CL is granted on the ground of failure to work or insufficient working.[27] There is no obligation under the TRIPS or the Paris Convention to give such cooling periods before the grant of a CL. There is an argument that in the case of medicines, this requirement may not be material, because the drugs get the marketing approval after 4-9 years from the date of grant of patents. However, it may not be true in all cases. At times, the patent holder may rely on a subsequent patent, even though the marketing approval is on the initial compound. In India, such situations arise because there are many patent applications in the mailbox and products are available in the market. Thus the cooling period of three years from CL delays the issuance of CL and favours the patent holder to enjoy the patent monopoly even in case of abuse of monopoly.

Further, the Act gives much discretion to the controller on the maintainability of the CL application. The controller is required to take certain facts into consideration while deciding the application for CL.[28] The grant of CL has to follow a cumbersome procedure. Both the Act and Rules do not prescribe any time limit for the conclusion of the proceedings. As a result, the final decision on the grant of CL can be the subject of indefinite delay. Certain exemptions with regard to procedural requirements are given if licence is requested on the grounds of national emergency, extreme urgency and public non-commercial use.[29] Even in such cases, the procedures under Section 87 of the Act normally apply.[30] It is the discretion of the controller to decide whether the procedures should be waived or not. Such delay in the case of emergency situations fails the purpose of CL. Another problem with the compulsory licensing provision is related to the intuitional remedy. According to Article 44 of TRIPS, there is no obligation on the part of member

27. Article 4 of Paris Convention.

28. According to Section 84(6) of the Patents Act, the following factors have been taken into account while granting CL. They include the nature of invention, the time, which has elapsed from the date of sealing of patent, and efforts by the patentee to make use of the invention; the ability of the applicant to work the invention to the public advantage; the capacity of the applicant to undertake risk in providing capital and working of the invention and including the efforts by the applicant to obtain the licence on reasonable terms and conditions within reasonable period of time. The reasonable period means six months from the date of request.

29. Section 92 of the Patents Act.

30. Section 92(2) of the Patents Act.

states to provide injunction as a remedy against case of government use. If provided, the patent holder may seek injunction to delay the use of patented invention under the government use. The Patent Act has not used this flexibility. As a result, any final decision regarding the use of a patented invention can be challenged in court and seek an injunction to stop the use of patented invention.

Further, the Patents Act does not provide ceiling on the royalty in case of CL and government use. The absence of ceiling on royalty may give rise to higher claims for royalty and related litigation. Thus the absence on ceiling on royalty brings great degree of uncertainty regarding the actual use of government use.

The above-mentioned gaps in the law take away the effectiveness of CL regime under the Patents Act. As a result, during the last five years, only one application was filed for the issuance of CL in India. It was filed under Section 92 of the Patents Act, which provides CL for exporting to countries which do not have the manufacturing capability in the pharmaceutical sector. This application was rejected by the Patent Office due to non-fulfilment of statutory requirement, i.e., the request from the importing country.[31]

There are only three applications that came up before the Patent Office for the issuance of CL during the post-TRIPS era. Patent Office rejected two applications citing lack of procedural requirements and granted one application. The decision to grant CL for Natco for a Bayer's patent was upheld by the Intellectual Property Appellate Board (IPAB). The reasoning of the Patent Office and IPAB clearly states that lack of local working means lack of local manufacturer. Further, the Patent Office and IPAB also invoked Section 84(1)(b) of the Patents Act, i.e., the patented article is not available at a reasonably affordable price to the public. However, these three cases confirms the above expressed fears with regard to the lack of time frame for the disposal of the CL applications as well as the wide discretion given to the controller of patents in the disposal of patent applications. The Natco case clearly brings out the absence of legal provisions in the determination of royalty.

31. See Patent Office decision dated July 4, 2008, POD/HK/2008-09/2942.

The above-mentioned uncertainties in the CL provisions coupled with an enabling policy framework which encourage the sue of CL prevents the Indian pharmaceutical manufactures to develop a business model that could use the CL to introduce the generic versions of patent-protected new medicines. Further, the current business model of many Indian pharmaceutical manufactures, which seeks strategic alliances including contract manufacturing with pharmaceutical MNCs, as well as urge to increase export to developed country market also act as a disincentive for the use of CL.

Government use is another most effective means to curb abuse of patents. It allows the government or its authorised agent to use the patents without the authorisation of the patent holder. Generally, the government can take over the patent invention without seeking a licence or to negotiate. This practice is available in most common law countries, especially in the US and the UK. In the UK, it is known as in the service of crown. In the US, it permits the government or its authorised person to use any patents on the ground of public use. The patent holder can sue the government only for compensation and no injunction remedy is available under the US law.[32] The advantage of government use is that it can bypass most of the procedural hurdles of the CL. However, the purpose of government use is restricted to non-commercial use. A country like India, with a public sector pharmaceutical industry, should strengthen the government use provisions in its Patents Act. The TRIPS provision on the government use is mentioned in Article 31(b) as public non-commercial use. It permits skipping requirements of voluntary licence and negotiating requirements. An important issue often raised is that when government use is non-commercial use, whether it is possible to sell through private channels. The answer is in the affirmative and government can recover the cost of production and distribution from non-commercial use. The affordability of drugs can be ensured through a strong government use provision (Indian context).

The Patents Act provides three types of government use. Firstly, a patent is granted in India with a condition that government can

32. See Correa (1999).

import the medicines for the distribution of drugs in public sector hospitals or any other hospitals to be notified in the gazette.[33] Secondly, government or authorised persons can use a patent against a royalty payment.[34] Thirdly, the central government can acquire a patent after paying compensation. Government can exercise these powers at any time.[35] However, the main lacuna is that the patented article under the Act can be sold only for non-commercial use.[36] This restriction may have far-reaching effect, because the courts may restrict the sales of medicines to public sector hospitals only. Further, the Act provides room for challenging the government decision to use or acquire the invention in the High Courts. It means the patentee can delay such use and the government has to prove need before the court. Using the TRIPS flexibility, the government should have opted for administrative review. The government has also failed to use the TRIPS flexibility with regard to removing injunction as a remedy in the case of government use.

Fearing the lack of political support, the Ministry of Health reduced its ambition of invoking government use under Section 100. The Ministry of Health has now formed a Committee which recommended three drugs to be notified under Section 92(1) of the Patents Act (Foot Note). A section 92(1) notification enables the CL applicant to obtain the licence without making effort to obtain the CL. However, the nodal ministry for the notification i.e., Ministry of Commerce and Industry has not made any notification.

Early Working

Early working exception permits the use of patents without prior permission for the purpose of obtaining regulatory clearance for production and marketing of a product. Thus the exception allows generic manufacturers to obtain the regulatory clearance well before the expiry of the patent and introduce the generic product in the market as soon as a patent expires. As a result, the patent holder

33. Section 47 of the Patents Act.

34. Sections 99 and 100 of the Patents Act.

35. Ibid.

36. Section 100 (6) of the Patents Act.

faces competition soon after the expiry of the patent. The Panel in the European Communities (EC)-Canada case confirmed it as an exception under Article 30.[37]

Section 107(A) (a) of the Indian Patents Act, prior to the 2005 amendment, permitted:

> Any act of making, constructing, using or selling a patented invention solely for uses reasonably related to the development and submission of information required under any law for the time being in force in India or a country other than India, that regulates the manufacture, construction use or sale of any product.

However, this provision unnecessarily puts several conditions like 'solely,' 'reasonably related,' etc., to use this exception. This imposes the burden of proof on the person using this exception. More importantly, it does not permit importation for regulatory purpose. As a remedy to some of these defects, the third Patent Amendment amended this section by permitting importation within the scope of exception. However, other conditions still remain. The patent holder may misuse these conditions to prevent generic manufacturers from using this exception.

Parallel Importation

This exception is based on the doctrine of exhaustion whereby the patent owner loses or 'exhausts' the right after the first sale of the patented product or a product produced through patented process. As a result, this exception allows another person to import the patented product without the permission of the patent holder from any other source, where the product is legally introduced in the market. However, the scope of this exception depends on the type of exhaustion regime allowed under the national law, *viz.*, international or regional or national exhaustion. Developing countries have absolute freedom to adopt international exhaustion under the Article 6 of TRIPS, and it would cease the control of the patent holder over the patented article with the first sale anywhere in the world (Correa, 2000: 75). In the other two cases, exhaustions

37. For a detailed discussion on Canada-EU, see Garrison (2006: 13-15).

happen only after the sale within the jurisdiction of a region or a nation. Article 6 of TRIPS states that issues of exhaustion of intellectual property (IP) should not be taken to WTO dispute settlement mechanism. Further, the Doha Declaration states that:

> The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment...[38]

There is liberty to member states to adopt a suitable exhaustion regime. Therefore, an international exhaustion principle is good for developing countries, because it enables them to import from anywhere in the world.[39] India enacted the parallel importation provision in 2002 by incorporating Section 107(A) (b) in the Patent Act. Under this section, parallel importation was permitted if the "importation of patented products by any person from a person who was duly authorised by the patentee to sell or distribute the product." The main lacuna of this provision is that it insists on authorisation from the patentee. As a result, one cannot import a product which is produced under compulsory licensing. This lacuna has been resolved in the 2005 amendment, which substituted words "who is authorised by the patentee to sell or distribute the product" with the words "who is duly authorised under the law to produce and sell or distribute the product."[40] Thus, now the drugs produced under CL can be obtained through parallel importation. However, the new provision also leaves some ambiguity by using the words produce and sell. In the strict sense, it means parallel importation cannot be done from a person who is legally authorised only to sell and not to produce. This is again an example of reducing the scope of parallel importation. In this way, India made use of the TRIPS flexibility to the fullest extent.

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38. Supra note 2, Paragraph 5(d).

39. Parallel importation may not be possible in the pharmaceutical sector, because the patent holders do not sell the product at different prices in different markets. Normally patent-protected medicines, with a few exceptions, are sold at same price internationally. Parallel importation would be useful only when the products are available at different prices in different geographical locations.

40. Section 107 (a) of the Patents Act.

Procedural Safeguards

TRIPS patent regime deals with the substantial law and therefore, member countries still have the freedom to regulate the procedural law. Therefore, procedural safeguards can be used to prevent the grant of frivolous patents. Procedures for the grant of patents should ensure a simple and transparent mechanism of granting the patent. Further, they should give room for public scrutiny of patent application because patent offices are not fully equipped to perform a thorough examination of patents. Even the US Patent Office with 3,000 examiners grants patents based only on the "preponderance of the evidence" [Federal Trade Commission (FTC), 2003]. Public scrutiny through a pre-grant opposition is necessary to check frivolous patents. TRIPS permits member countries to have reasonable procedures and formalities consistent with it for the acquisition and maintenance of intellectual property.[41]

However, the 2005 amendment diluted the procedural safeguards in the Indian Patents Act. There were three stages of granting a patent: (i) initial publication after 18 months of filing; (ii) acceptance of complete specification after the examination and scrutiny by the patent office; and iii) publication of the accepted complete specification inviting opposition from the public. The 2005 amendment removed the last two stages procedure prior to the granting of patents. Presently a patent applicant obtains all privileges of patent except the right to sue for infringement immediately after the first publication, i.e., after 18 months from the date of publication. As a result, the privileges of patent except the right to file infringement suit are available even without examination of patent application. Further, patents office grants the patents immediately after the examination and there is no acceptance of complete specification before the grant of patents. As per the ordinance, the time frame for making the examination report is left to the rules. The new rules under the Patents Act provide 1-3 months for the examination report preparation changing the earlier 18 months period. The third amendment also took away another

41. Article 62 (1) of TRIPS.

important check against frivolous patents provided in Section 27 of the Patents Act which gave powers to the controller to take *suo moto* steps to refuse grant of patent on ground of anticipated publications. Hence, the amendment diluted the process to favour the patent applicant.

The amendment has restored the pre-grant opposition of patent applications. There are 11 grounds on which one can file opposition and seek recourse to challenging frivolous and legally invalid patents.[42] However, still the opposition is by way of representation and not in the form of notice to opposition, where it opens an *inter partes* procedure. It was also not clear in the beginning whether the opponent could access the documents on which the patent holder relies on the claim or the evidence furnished by patent applicant to support the claim. Furthermore, there is no scope for appeal against the decision of the controller on the representation to oppose the patent. However, in the Novartis case, the Madras High Court allowed Novartis to approach the Appellate Board against the decision of the pre-grant procedure, which rejected its patent application for Chronic Myeloid Lukemia (CML).

The effectiveness of the opposition process depends upon the ability to access information on the patent applications. The patent office does not publish the complete specification before the grant of patent. This lack of publication takes away the possibility of accessing information relating to the patent application and the ability to oppose the same. This would greatly hamper opposition proceedings. The amendment also provides post-grant opposition within one year from the date of publication on the grant of patent. The grounds are similar to pre-grant opposition in this aspect. However, the post-grant opposition suffers from institutional bias. Under the post-grant procedure, there would be a board to hear the application but the controller of patents makes the final order. The controller is not bound by the decision of the post-grant opposition board.

Generic companies and public interest groups are using pre-grant opposition provisions to prevent frivolous and evergreening patents.

42. Section 25 (1) of the Patents Act.

Since January 1, 2005, to March 31, 2009, approximately 458 pre-grant oppositions have been filed in various patents offices against 390 patent applications.[43] Majority of these pre-grant applications are currently undergoing various stages of pre-grant opposition procedure. However, a recent study claims that only 34 decisions on pre- and post-grant oppositions have been given between 2005 and 2008 (Unnikrishnan, 2009). Out of these 34 decisions, 33 are on pre-grant opposition and 1 is on post-grant opposition. Further, the study also states that 25 out of 34 resulted in the rejection of patent applications. However, the number of pre-grant oppositions filed is showing a decline. The Patent Office received only 193 pre-grant in the year 2011-12 against 294 in 2010-11. The number of disposal of pre-grant opposition is very low. Only 11 pre-grant oppositions applications were disposed in 2011-12. Similarly, only 16 post-grant oppositions were disposed and 155 were pending in 2011-12. This delay in disposal of pre-grant application would affect the utility of pre- and post-grant opposition mechanisms.

This shows that there is an under utilisation of the pre- and post-grant opposition. Various reasons can be attributed for this under utilisation of the pre- and post-grant provisions including barriers in accessing the information, especially identifying the right application from the pile of thousands of patent applications, lack of cost-effective human resources, lack of awareness and capacity deficit among generic companies, especially small and medium enterprises, etc. Further, this low number of pre- and post-grant opposition exposes the propaganda of pharmaceutical MNCs that the interested parties misuse the pre-grant opposition to delay the grant of patents (Unnikrishnan, 2007).

Licensing Agreements

Licensing is the most effective way of transferring a patented technology. The licensing agreement can provide certain conditions which affect the purpose of transfer technology. Licensing agreements are important because TRIPS promotes voluntary licensing by making evidence of efforts to obtain voluntary licence

43. Lok Sabha, Unstarred Question No. 2784 dated December 7, 2009.

before applying for compulsory licence. Therefore, regulation of licensing agreements is critical to promote the transfer of technology, which is explicitly mentioned as one of the principles of TRIPS. TRIPS does not prevent members from specifying in their legislation licensing practices or conditions that may in particular cases constitute an abuse of Intellectual Property Rights (IPRs) having an adverse effect on competition in the relevant market. Further, it obligates members to engage in consultation if the intellectual property (IP) owner belonging to one country indulges in practices that violate the regulations on licensing agreements and *vice versa*.

The Patents Act declares certain provisions in the licence agreement as unlawful if it contains the following clauses:[44] exclusive dealing on non-patented article, use of a non-patented article other than that supplied by the licensor, use of any process other than the non-patented process and exclusive grant back. As mentioned above, the coercive conditions in the licence are a ground for CL. The Patents Act does not link these clauses with CL or anti-competitive remedies. It mentions that these can be used as a ground against infringement proceedings.[45] During the last five years, the patent holders granted at least three licensing agreements containing anti-competitive provisions to Indian generic manufactures.[46] However, the patent office could not scrutinise those licencing agreements in the absence of patent in force. Licencing agreements were granted on the basis of a pending patent application.

The growing number of voluntary licences of patented medicine increases the critical role of this provision of the Patent Act to check anti-completive licencing practices of the patent owners. However, there is no information in the public domain whether the Patent Office has scrutinised any licencing agreements.

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44. Section 140 of the Patents Act.

45. Section 140(3) of the Patents Act.

46. In 2005, Roche issued a voluntary licence to Indian pharmaceutical company Hetor to produce its avian flue medicine Oseltamivir. In 2006, Giled Sciences granted voluntary licence to nearly seven Indian companies to produce Tenofovir (TDF), an anti-retroviral (ARV) drug for HIV/AIDS treatment. In 2006, Bristol Myers Squibb (BMS) issued another voluntary licence to Indian pharmaceutical company Emcure to produce Ataznavir, another ARV drug for the treatment of HIV/AIDS.

The above discussion clearly shows that Indian Patents Act contains most of the TRIPS flexibilities. However, the provisions containing the flexibilities fail to clarify critical questions associated with the TRIPS flexibilities. As a result, most of the flexibilities contained in the Patent Act suffer from the following shortcomings. First, the legal provisions related to flexibilities give room for interpretations by the administrative and judicial authorities, which may at times go against the very legislative intent of the provisions, for instance, litigation on the constitutional validity of Section 3(d). In a common law country like India, it is important to avoid the interpretational freedom because the judicial interpretation sets precedents and legal validity. Second, some of the legal flexibilities, especially related to the scope of patent protection, give a case-to-case application of law and drastically reduce the utility in practice. For example, the application of Section 3(d) is often overlooked and patents are granted on patent applications claiming patents contrary to Section 3(d). Further, it also needs expert human resources to implement these flexibilities and requires additional resource for the human development. Third, the use of flexibilities would be hampered due to the extensive procedural requirements involved in the invocation of those flexibilities like CL. Fourth, the provisions related to flexibilities do not curtail the avoidable litigation with regard to the issuance of compulsory licence and government use, etc. This creates uncertain outcomes with regard to the actual operation of flexibilities like CL and hampers the practical use of these mechanisms.

Apart from the above-mentioned legal constraints, the following policy constraints too prevent the use of flexibilities in the Patents Act. In other words, there is no policy framework which encourages the Indian pharmaceutical manufactures to make use of flexibilities. The following section highlights some of these policy constraints.

Policy Constraints

As mentioned in the beginning, supportive policy framework plays a critical role in the successful implementation of TRIPS flexibilities. The policy framework should aim at providing incentive for generic pharmaceutical industry to meet the

challenges of product patent regime. Policy response can either facilitate the integration of Indian generic industry within the IP framework or enhance the capacity of generic industry to use the TRIPS flexibilities including research exception, patent pre-grant opposition, compulsory licensing, etc., and contain the monopoly power of pharmaceutical MNCs emerging out of product patent regime. The following paragraphs examine the policy responses of selected government departments to TRIPS patent regime.

Three major policies in the post-TRIPS scenario, *viz.*, National Pharmaceutical Policy 2002, National Health Policy and Science and Technology Policy 2003, recognised the challenges of enhanced IP protection. The preamble of the Science and Technology (S&T) Policy states that:

> Science and technology have had unprecedented impact on economic growth and social development. Knowledge has become a source of economic might and power. This has led to increased restrictions on sharing of knowledge, to new norms of intellectual property rights and to global trade and technology control regimes.[47]

However, the policy response to this concern is exactly opposite. One of the policy objectives of S&T is:

> To establish an Intellectual Property Rights (IPR) regime which maximises the incentives for the generation and protection of intellectual property by all types of inventors. The regime would also provide a strong, supportive and comprehensive policy environment for speedy and effective domestic commercialisation of such inventions so as to be maximal in the public interest.[48]

This policy objective clearly shows that government is focusing on generation and protection of IP instead of addressing the concern expressed in the preamble. Further, the objective is focusing on the commercialisation of inventions rather than its dissemination. Again, the operational part of the policy states that:

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47. Available at <*http://www.dst.gov.in/stsysindia/stp2003.htm*>, accessed on October 10, 2009.

48. Ibid.

> our legislation with regard to patents, copyrights and other forms of intellectual property will ensure that maximum incentives are provided for individual inventors and to our scientific and technological community, to undertake large scale and rapid commercialization, at home and abroad.[49]

Thus, the S&T Policy considers IP protection as the main means of IP commercialisation. It is silent on the implications of high-level IP protection, especially on the research and development (R&D) and dissemination of technology. The same stand is repeated in 2013 Science, Technology and Innovation Policy. There is nothing in the policy to encourage the use of flexibilities to increase access to medicines.

The health policy also recognises the challenges of the product patent protection. It states that:

> There are some apprehensions about the possible adverse impact of economic globalisation on the health sector. Pharmaceutical drugs and other health services have always been available in the country at extremely inexpensive prices. India has established a reputation around the globe for the innovative development of original process patents for the manufacture of a wide-range of drugs and vaccines within the ambit of the existing patent laws. With the adoption of Trade Related Intellectual Property Rights (TRIPS), and the subsequent alignment of domestic patent laws consistent with the commitments under TRIPS, there will be a significant shift in the scope of the parameters regulating the manufacture of new drugs/vaccines. Global experience has shown that the introduction of a TRIPS-consistent patent regime for drugs in a developing country results in an across-the-board increase in the cost of drugs and medical services. NHP-2002 will address itself to the future imperatives of health security in the country, in the post-TRIPS era.[50]

However, the policy proposes a very general policy measure to address the challenge.

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49. Ibid.

50. Available at <*http://www.mohfw.nic.in/np2002.htm*>, accessed on September 23, 2009.

> The Policy takes into account the serious apprehension, expressed by several health experts, of the possible threat to health security in the post-TRIPS era, as a result of a sharp increase in the prices of drugs and vaccines. To protect the citizens of the country from such a threat, this policy envisages a national patent regime for the future, which, while being consistent with TRIPS, avails of all opportunities to secure for the country, under its patent laws, affordable access to the latest medical and other therapeutic discoveries.[51]

The Ministry of Health just leaves the challenges of product patent regime to the patent laws, a serious issue only to be handled by the Ministry of Commerce and Industry, which is in charge of administration of patents. The health policy is silent on the concrete measures to be taken in the case of deficiency in access to medicines due to patent protection.

The Indian pharmaceutical sector underwent a major policy shift with the economic liberalisation project since the 1990s. As a result, 100 per cent foreign investment in pharmaceutical sector has been permitted through automatic route. The public sector drugs and pharmaceutical manufacturing were exposed to competition, including competition from imports. Majority of public sector manufacturing units were closed down. Against this background, the government introduced the Pharmaceutical Policy 2002.[52] The Policy clearly identifies the challenge when it states that "two major issues have surfaced on account of globalisation and implementation of our obligations under TRIPS which impact on long term competitiveness of Indian industry."[53] Towards facing the challenge, the policy proposes a reorientation of objectives, *viz.*, improving incentives for R&D in the Indian pharmaceutical industry, to enable the industry to achieve sustainable growth, particularly in view of anticipated changes in the Patent Law and reducing further the rigorous price control. Thus reducing the number of price-controlled drugs was the main response to meet the challenge of patent.

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51. Ibid.
52. Available at <*http://pharmaceuticals.gov.in*>, accessed on September 23, 2009.
53. Ibid.

However, this proposal of reducing the number of drugs under price control was stayed by the Supreme Court. The proposal would have resulted in the reduction of number of price-controlled drugs from 74 to 34. The Court instructed the government to "consider and formulate appropriate criteria for ensuring essential and life saving drugs not to fall out of price control" (Narrian, 2004). In fact, price control is one of the flexibilities available under TRIPS to ensure public access to medicines. Nothing in TRIPS prohibits member countries from controlling the prices of patented drugs.

There is nothing in the National Pharmaceutical Pricing Policy 2012 to make use of flexibilities in the Patents Act such as compulsory licence.

The latest policy and its corresponding Drug Price Control Order are silent about the price control of patented medicines. Instead of price control, the policy proposes price negotiation. Towards this purpose, a new committee has been appointed in 2013 rejecting the draft report of an earlier committee set up in 2007. The objective of the committee is to explore the possibility of price negotiations for patented drugs and medical devices before the granting proposal (Mukherjee, 2007). The new committee is yet to come out with its recommendations. Instead of controlling the prices of patented drugs in the proposed mechanism, negotiations would be carried out with the patent owner. This would give much leeway to the patent holder to set a high price. Often the price of the patented article is extremely high and there will not be sufficient price cut through negotiation. Further, it may undermine the compulsory licence option. For instance, under the Indian Patents Act, high price of patented article constitutes a ground for granting CL. Hence, if the price for the patented article is high, then generic companies can approach the authorities for a CL citing the high price of the patented medicine. This option would be undermined through a price negotiation mechanism, wherein a negotiated token price cut would be treated as a legitimate reasonable price.

Further, the new policy allows exemption from price control of 343 drugs contained in the National List of Essential Medicines (NLEM) if there is a product or process patents on these drugs.

Thus the new policy encourages patenting of essential medicines, which are often old drugs and therefore not supposed to obtain product patent protection under the Indian Patents Act.

The foreign direct investment (FDI) policy in pharmaceutical industry is also acting as a threat to the use of flexibilities. The FDI policy till 2012 allowed 100 per cent FDI in pharmaceutical manufacturing without any restrictions on both brownfield and greenfield investments. This lack of clarity has facilitated acquisition of major Indian pharmaceutical manufactures with technological capabilities by MNCs. This growing control of MNCs on Indian pharmaceutical sector would pose threat to the use of flexibilities. The modified policy, which demands prior permission for the brownfield investment, which was introduced in 2012, failed to check the MNC acquisition of Indian generic companies. Realising this threat, the Parliamentary Standing Committee on Commerce recommended a blanket ban on brownfield investment in pharmaceutical sector.

Apart from the above-mentioned policy constraints, the following moves by the government also bring uncertainties with regard to the future policy space for the use of flexibilities.

Another move of the government, which gives conflicting message on the using of TRIPS flexibilities, is the move to implement data exclusivity. Under Article 39 of the TRIPS Agreement, there is no obligation to provide data exclusivity. If implemented, data exclusivity prevents national drug regulatory authorities from approving generic medicines on the basis of test data generated by the originator companies for a fixed period of time. Hence, implementation of data exclusivity prevents the introduction of generic drugs even in the absence of patent protection. Further, data exclusivity may frustrate the issuance of compulsory licence. A report submitted by the then Secretary, Department of Chemicals, recommended the progressive implementation of data exclusivity.[54]

Similarly in 2008, the Drugs Control General of India (DCGI) attempted to introduce patent linkage. This would have prevented

54. Available at <*http://chemicals.nic.in/DPBooklet.pdf* >, accessed on September 28, 2009.

the registration of a generic company from obtaining marketing approval of a patented medicine (Mathew, 2008a). This would have made the DCGI's office to become the *de facto* authority for the enforcement of patents. Since multiple patents are obtained on single medicine, it is really impossible for the DCGI's office to find out the relevant patent and deny marketing approval. It would also prevent generic competition. The most important fact is that patent linkage is a TRIPS plus obligation and reduces the policy space for the TRIPS flexibilities.

Another important initiative, which may neutralise strategies on the TRIPS flexibilities, is the engagement on free trade agreements (FTAs) (Jishnu, 2009a). India is currently engaged in more than 27 FTAs and some of these engagements are at various stages of negotiations. Three of these FTA negotiations with Japan, the European Union (EU) and European Free Trade Association (EFTA) include IPRs. The leaked text of the EU-India FTA shows that the EU is demanding data exclusivity and extended terms of protection from India. The already concluded FTAs with EFTA also contain similar TRIPS plus provisions. The FTAs with Japan also contain TRIPS plus provisions including data exclusivity, patent extension and limitation on compulsory licence.

Thus, the policy responses do not address the challenges of product patent regime. Instead, as mentioned above, the S&T Policy and Pharmaceutical Policy not only recognise patent, but also encourage IP protection rather than coming up with policy tools to face the challenges of product patent regime. Some of the policy initiatives give a confusing signal on the intention of government on using the flexibilities available under the TRIPS Agreement and make Indian state vulnerable to pharmaceutical MNC and their host states pressure for implementing law and policy that minimises the scope of TRIPS flexibility. Further, the lack of clear cut policy framework prevents generic pharmaceutical industry from developing a viable business model using TRIPS flexibilities.

Institutional Constraints

The patent office plays a crucial role in the implementation and utilisation of the TRIPS flexibilities, especially those during the pre-

grant stages of the patent. The pre-grant flexibilities in the TRIPS can be effectively used to minimise the number of patents granted. As mentioned earlier, India incorporated these flexibilities to mainly curb the practice of patenting of known substances. It is for the patent offices to apply these flexibilities while examining the patent applications and to decide whether the patents are to be granted or not. To address these challenges, the Indian Patent Office took certain concrete measures including the patent office modernisation, expansion of human resources and patent automation. However, some of these measures do not complement the implementation of the TRIPS flexibilities.

In order to streamline the patent examination process, Patent Office redrafted a new patent office manual. This new manual incorporated the changes in the Patents Act, especially the provisions related to patentability criteria. The manual is supposed to serve as a reference for the patent examiner to apply the law in the real contexts. Thus it plays a crucial role in influencing the decision of the patent examiner, even in the absence of a legal sanctity compared to the Patent Act and Rules. In other words, the Patent Office manual is to reflect the legislative purpose and spirit. However, the new manual developed by the Patents Office is drawn from examples and case laws from European and the US jurisdictions.[55] Thus, the instruction to the patent examiners in the manual reflects the jurisprudence of EU and US patent law rather than the legislative intentions of the Indian patent law.

Indian Patents Act set different standards for the patentability criteria including Section 3(d), but the manual does not reflect those differences. However, some of the instructions contained in the patent manual directly bypass the provisions of the Act. For instance, Section 3(d) states that salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy. Hence, the patent

55. Available at <*http://ipindia.nic.in/ipr/patent/DraftPatent_Manual_2008.pdf*>, accessed on October 15, 2009.

examiner should treat all the above-mentioned items as known substance, unless they differ significantly in properties with regard to efficacy. The burden of proof is on the patent applicant to prove that the patent claim on known substance is different in efficacy. In other words, the patent examiner has no discretion to decide otherwise, without examining the efficacy element. However, the patent manual states "Isomers having the same empirical formula but having structural differences may be considered novel and may not normally offend "obviousness" as they are structurally different."[56] This statement instructs the examiner to ignore the legislative requirement on efficacy and accepts claim on an isomer having structural difference therefore eligible for patent protection. Thus the Patent Office manual bypasses the provisions of the Patents Act.

In order to enhance the capacity, the Patent Office entered into eight Memorandum of Understandings (MoUs) with the developed countries.[57] All these eight countries are advocates of enhanced patented protection and compromise the strict patentability standards. These MoUs cover human resource development, capacity building activities, exchange of best practices and information exchange. This would lead to importation of the developed country practices through examination process and training of examiners. For instance, the Patent Office MoU with the US Patent Office (USPTO) states that:

> The Parties shall work together in capacity building in Intellectual Property Rights including automation and modernisation of Intellectual Property Offices, development of databases, and procedural rationalisation and simplification of processing of Intellectual Property applications, inter alia, through the exchange of information on patent data, best practices in patent examination procedures, etc.
>
> The two Parties shall cooperate in the training of personnel and human resource development in the area of Intellectual Property Rights with a view to strengthening the working of

56. Ibid.: 59.

57. Indian Patent Office signed MoUs with IP or patent offices of Australia, Germany, Switzerland, Japan, the UK, the US, France and the European Patent Office (EPO).

the Intellectual Property (IP) systems in the two countries, including in patent examination training.[58]

As part of the MoU, nearly many patent examiners were trained under USPTO. Hence the manual brings a backdoor harmonisation of patent examination standards with the US and the EU patent examination practices.

After the conclusion of the TRIPS Agreement, developing countries like India witnessed a sudden increase in the patent applications. Pharmaceutical MNCs started filing product patent applications in developing countries especially in India with the objective of blocking the introduction of generic medicines. As a result, there is a four-fold increase in the number of patent applications filed in India from 1996-97 to 2007-08. During 1996-97 the patent office received 8,562 applications and the number of applications increased to 35,218 during 2007-08 (Office of the Controller General of Patents, Designs and Trademarks, 2008: 22). There is a similar increase in the number of applications examined by the Patent Office. The number of examined applications rose from 3,042 in 1996-97 to 11,751 in 2007-08 (Ibid.: 4). The number of granted patents also increased the same way. Granted patents increased from 907 in 1996-97 to 15,261 in 2007-08, almost an increase of 17 times (Ibid.: 6).

Out of the 35,218 applications filed during 2007-08, only 6,040 applications originated in India (Ibid.). In other words 83 per cent of these applications came from foreign countries. Majority of foreign applications come through the Patent Cooperation Treaty (PCT) route. During 2007-08, Patent Office received 23,891 patent applications through PCT route (Ibid.: 7). The largest number of patent applications originates from the US, which accounted for 8,606 applications through PCT route during 2007-08. Germany with 2,441 and Japan with 1,806 applications are in the second and third place respectively (Ibid.: 22). Out of the 15,261 granted patents, 12,088 applications were granted to the foreign nationals. Only 3,173 patents were granted to Indian nationals (Ibid.: 7).

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58. Articles 3 and 4 of MoU on bilateral cooperation between Controller General of Patents, Designs and Trademark and the United States Patent and Trademark Office, available at: <*http://dipp.nic.in/acts/MOU_of_bilateral_cooperation_with_usa.pdf*>, accessed on October 25, 2009.

The breakup of patent applications shows that out of 35,218 patent applications filed during 2007-08, 4,267 applications were on drugs (Ibid.). The applications on drugs included pharmaceutical and agro-chemical applications. The largest number of applications was in the field of chemicals (6,375) (ibid.) Applications on biomedical and biochemistry were 879 and 1,190, respectively. During the same period, 4,071 patents were granted in the field of chemicals and 1,469 patents on drugs. The number of granted patents on chemicals and drugs during 2006-07 were 1,989 and 798, respectively (Ibid.).

However, there is a mismatch between the number of granted patents and the number of examiners. There are only 163 professionals working at the Patent Office, who are capable of performing patent examination. These 163 examiners are having different specialisations. There are 62 patent examiners having specialisations in chemistry (31), biotech (11), microbiology (11), biochemistry (8) and biopharma (1), who are capable of examining patents on pharmaceuticals and health-related technology. These 62 examiners have granted 7,166 patents during 2007-08. The breakup of 7,166 patents is: chemicals (4,071), drug (1,469), biochemistry (91,149), biotech (314), biomedical (138) and microbiology (25). This shows that each examiner granted 155 patents in 2007-08. This work burden often results in the grant of patents without proper scrutiny (Ibid.).

Judiciary is the other important institution playing a critical role in shaping scope of protection and public interest safeguards contained in the Patents Act. As noted above, the provisions of the Act provide lot of space for interpretation and each time judiciary plays the role of final arbitrator on dispute related to interpretation of law and facts. During the last five years, courts examined three important issues with regard to the patent law. As mentioned earlier, the Madras High Court dismissed the petition of Novartis, which challenged the constitutional validity of Section 3(d) of the Patents Act. In another case, the single bench and division bench dismissed a petition by Holfman Roche seeking the preliminary injunction against the generic manufacturing company

from producing anticancer drug erlotinib. While dismissing the preliminary injunction, the single bench noted that:

> The court is of the opinion that as between the two competing public interests, that is, the public interest in granting an injunction to affirm a patent during the pendency of an infringement action, as opposed to the public interest in access for the people to a life saving drug, the balance has to be tilted in favour of the latter. The damage or injury that would occur to the plaintiff in such case is capable of assessment in monetary terms. However, the injury to the public would be deprived of the defendant's product, which may lead to shortening of lives of several unknown persons, who are not parties to the suit, and which damage cannot be restituted in monetary terms, is not only uncompensatable, it is irreparable.[59]

The division bench of the Delhi High Court while dismissing the appeal against the order of the single bench found that the petitioner, i.e., Roche, agreed with the single judge on the question of public interest while issuing the injunction. The division bench held that:

> The question of general public access in our country to life saving drugs assumes great significance and the adverse impact on such access which the grant of injunction in a case like the instant one is likely to have, would have to be accounted for. This Court finds no ground to differ with the reasoning or the conclusions arrived at by the learned Single Judge on this aspect.[60]

The division bench also found that the petitioner suppressed material facts and failed to disclose the complete invention. Therefore, the court dismissed the petition with cost and ordered to pay the defendant ₹ 500,000 (USD 10,743).[61]

The third important case disposed by the Delhi High Court is with regard to Bayer's writ petition seeking court intervention to prevent the DCGI from issuing manufacturing licence to generic

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59. F. Hoffmann-La Roche and another *versus* Cipla Limited (I.A 642/2008 IN CS (OS) 89/2008), dated March 19, 2008, p.61.

60. F. Hoffmann-La Roche and another *versus* Cipla Limited (FAO (OS) 188/2008) dated April 24, 2009, p.54.

61. Ibid.: 57.

companies for patented medicine. This was an attempt to establish patent linkage in India through court orders to prevent the issuance of manufacturing licence for patented medicines. This would have turned the DCGI a *de facto* enforcing authority for patented medicines. Such a linkage between patent and drug registration would have undermined the TRIPS flexibilities like early working (Bolar provision), parallel importing and compulsory licence. While dismissing the writ petition with the cost of ₹ 600,000 (USD 12,892) to be paid to the respondents, the court remarked that:

> This court is constrained to observe that the present litigation was what may be characterised as a speculative foray; an attempt to "tweak" public policies through court mandated regimes. The petitioner doubtless is possessed of vast resources and can engage in such pursuits. Yet, often, these attempts, even unsuccessful in the ultimate analysis, achieve short-term goals of keeping out competitors, through interim orders. That short term objective has been achieved, and the petitioner has successfully stalled an independent examination of Cipla's application.[62]

Recently, the division bench of the Delhi High Court affirmed the decision of the single bench.[63]

However, the disturbing information is regarding the attempts of IP protection lobby to influence the judiciary with expectation of securing favourable judgment. The academic and corporate organisations based in the US primarily coordinate this lobby. Since 2003, the George Washington University (GWU) Law School coordinates an IP lobby programme known as the India Projects. Under this project, GWU coordinates an annual lobby visit of a US delegation consisting of pro-IP academic, corporate executives and judges of Federal Circuit Courts.[64] This delegation meets the judges of High Courts and the Supreme Court to advocate the need

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62. Bayer Corporation and others *versus* Union of India and others (WP(C) No.7833/2008), dated August 18, 2009, p.31.

63. Bayer Corporation *versus* Union of India , LPA 443/2009.

64. For a brief description of the India Project, see <*http://www.law.gwu.edu/Academics/research_centers/india/Pages/Overview.aspx* >, accessed on October 31, 2009. Also see the interview of the Dean of GWU Law School, available at: <*http://www.law.gwu.edu/Academics/research_centers/india/Documents/India_article.pdf*>, accessed on October 31, 2009.

for strong IP protection.[65] Further, Indian judges were invited to attend the conferences organised by the pro-IP lobby abroad.[66] This pro-active lobbying with judiciary may have adverse impact on the scope of public interest safeguards in the Patents Act.

Another institutional gap is with regard to the issuance of CL and the government use. Section 92 of the Patents Act contains certain exceptional circumstances under which procedural requirements for the issuance of CL can be waived. This section can be invoked only on the basis of a declaration to issue a CL in national emergency or extreme urgency or public non-commercial use. Similarly, under Section 100, central government has the power to use the inventions for purposes of government. However, there is no institutional mechanism within the government to monitor the impact of patented drugs on access to medicine and invoke timely measures like CL or government use provisions in the Patents Act. This institutional gap would delay the invocation of government use provision for meeting the public health needs of the country.

The above discussion shows that the institutional support required for the effective use of public interest safeguards is not adequate in India. Patents Office suffers from quality human resources and transparency. Its ability to apply the patent law to the Indian context will be seriously challenged by the importation of jurisprudence from the US and the EU patents offices. Some of the progressive signs shown by the judiciary may be hampered by the constant lobbying by the pro-IP lobby consisting of academics and corporate.

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65. The Programme brochure shows that on February 22, 2009, this delegation had programme titled "Dialogue with Judiciary." Soft copy of the brochure is with the author. The 6th visit was jointly organised by the US-India Business Council, GWU Law School and the Confederation of Indian Industry (CII).

66. Two of the Indian Supreme Court Judges attended the International Judges Conference, April 20–21, 2009, Washington, DC. This conference was organised by the IP Owner's Education Foundation promoted by the IP Owner's Association, a pro IP lobby claiming to serving the intellectual property community in the US and worldwide. To see the list of participants visit: *<http://www.ipo.org/AM/Template.cfm?Section=International_Judges_Conference&Template=/CM/ContentDisplay.cfm&ContentID=22075>*, accessed on October 31, 2009.

Conclusion

The above discussion clearly shows that there is a legal, policy and institutional deficit in the implementation of the TRIPS flexibilities in India. Even though the Indian Patent Act contains all the TRIPS flexibilities, the relevant provisions require further fine-tuning, especially of those related to scope of patent protection, CL and government use. The current provisions provide space for legal interpretation of critical areas like the scope of patent protection. This may result in an interpretation, which is contrary to the original purpose. Further, the provisions like CL and government use involve cumbersome legal procedures and neutralises the practical use of public interest safeguards. Hence, amendments to the existing provisions on scope of patentability and CL are required for the effective implementation of the TRIPS flexibilities.

The incorporation of the TRIPS flexibilities in the domestic law has to be complemented through sound policy measures to facilitate the actual use of the public interest safeguards provided in the law. While the key policy documents acknowledge the challenges of intellectual property regime, the policy prescriptions are directed to the exact in the opposite direction. Further, there is no policy initiative to facilitate the implementation of public interest safeguards like pre-grant opposition, government use, etc. On the contrary, many policy initiatives of the government like the inclusion of IPR in FTA negotiation and the Satwant Reddy Committee recommendation to implement data exclusivity in the long run, etc., go against the very idea of public interest safeguards and eliminate use of the TRIPS flexibilities. These contradictory policy measures create confusion among the potential users, especially generic industry, to develop a long-term strategy on the basis of the flexibilities available in the Patents Act.

There is also a capacity deficit among institutions like the patent office and judiciary, which are supposed to play the critical role in translating the flexibilities into practice. The institutional response of the patent office to meet the challenges of product patent regime is often slow and short of expectation. There is evidence to show the granting of patents on old molecules. This shows

the capacity deficit of patent office in applying the safeguards against patenting of known substances (evergreening). Some of the responses of patent office to meet the challenge of product patent regime are also not in the right direction, for instance, MoUs with developed country patent offices to train patent examiners. There is no institutional mechanism to assess the impact of the patents on access to medicine, which is important to invoke CL and government use.

Policy concerns on access to affordable medicines demand changes in these three areas: (i) fine-tuning of the relevant provisions of the Patent Act; (ii) sound policy measures; and (iii) capacity building of institutions like the patent office and judiciary. Mere incorporation of the TRIPS flexibilities in the domestic legislation alone is not enough to address the concerns of access to medicines. The flexibilities in the domestic patent law should be complemented with sound policy measures and institutional support. Such complementary policy measures and institutional support require investment in financial and human resources, which most of the developing countries cannot afford.

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Rational Use of Medicines in India

Introduction

One of the critical areas of access to medicines is the issue of rational medicine use. Irrational medicine use can occur at every stage of the drug cycle, from production of the medicine, through prescription and dispensing by medical professionals, to use of the medicine at the patient level. According to the World Health Organization (WHO), "The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and at the lowest cost to them and their community."[1]

Irrational medicine use can produce poor clinical outcomes for patients as well as a higher financial burden to individuals, families and society. The drug market is characterised by "information asymmetry". Typically, medicine prescribers (doctors, pharmacists, druggists, etc.) are targeted by the drug manufacturers to promote their products irrespective of evidence on the efficacy and effectiveness of the molecules marketed. The concept of rational drug use has taken a backseat in spite of the availability of Essential Drug Lists (EDL) and Standard Treatment Guidelines (STG), due to high-voltage promotional practices, poor regulatory framework and even poorer enforcement of existing acts and rules. As a result, drugs are acting as cost drivers of health care without any measurable impact on health improvements. Also, public procurement of

1. World Health Organisation (1985).

irrational drugs can act as a major cost barrier resulting in lack of other essential medicines that are most needed in the system.

The Availability of Non-Essential Medicines

Drug companies often produce non-essential medicines which they promote assiduously without any regard for the health of the individuals and society and the associated costs. Such drugs and their use could result in death and disability besides inflicting substantial financial burden on households. Non-essential medicines are categorised into three broad headings:

- Banned/bannable drugs.
- Irrational fixed dose combinations (FDCs).
- Medicines with unproven/dubious efficacy.

Banned and Bannable Drugs

Several medicines that are considered unsafe and often banned in other countries are sold and prescribed by physicians and dispensed by chemists in India. In such cases, the likelihood of adverse reactions outweighs the therapeutic effects. The safety of the patients is therefore compromised with the ultimate motive of profit-seeking. In view of the lax drug regulatory system in the country, drug makers have been able to bypass the ban and sell such medicines unhindered.

The use of anabolic steroids for growth and appetite stimulants in children and athletes is one common example. While most developed countries have banned the use of dipyrone (metamizole), it is freely available in India and used indiscriminately in both health facilities and the community for minor ailments. Major medicines that are banned globally but still sold in India include:

- Nimesulide, which is used as a painkiller or in conditions of fever, is considered to be hepatotoxic.
- Analgin is used indiscriminately, which is likely to cause bone marrow depression in patients.
- Cisapride, a drug used in acidity or constipation, is feared to cause irregular heartbeats.

- Furazolidone, which is used in patients as an anti-diarrhoeal, is apprehended to be carcinogenic.
- Piperazine, an anthelmintic, is expected to cause nerve damage.
- Nitrofurazone, which is utilised as antibacterial cream, is feared to be carcinogenic in nature.

Fixed Dose Combinations

According to a WHO (2005) technical report, a fixed dose combination is defined as "a combination of two or more active ingredients in a fixed ratio of doses. This term is used generically to mean a particular combination of APIs [active pharmaceutical ingredients] irrespective of the formulation or brand. It may be administered as single entity products given concurrently or as finished pharmaceutical products."

Four scenarios could be visualised for a drug maker to produce an FDC:

i) The new FDC contains similar APIs in the same doses as an existing FDC.

ii) The new FDC contains the same APIs in the same doses as an established regime of single entity products and the dosage regimen is the same.

iii) The new FDC combines APIs not previously combined for this indication or used in different dosage form.

iv) The new FDC contains one or more new chemical entities.

In all such scenarios, the safety and efficacy profile of new FDCs must be ensured. In determining whether it is rational to combine two or more APIs into a single product, medical, quality and bioavailability considerations need to be taken into account while accepting the registration of any new FDC. One of the advantages of FDCs is the combination therapy they provide to patients while reducing the number of pills to be taken separately. Improved patient adherence is likely to ensue with FDCs, as it reduces the number of pills consumed at a time. This is especially

true in conditions relating to chronic diseases, where partial adherence is expected to develop drug-resistant strains, which could result in treatment failure. In some instances, it is expected that a combination of two APIs could reduce the side-effects of one medicine. For example, carbidopa is likely to reduce the side-effects of levodopa. Proponents of FDCs also claim that the efficacy of one API can be synergistically enhanced while combining with another API, e.g., the combination of estrogen and progesterone in oral contraceptives, and the combination of pyrimethamine and sulfadoxine for the treatment and prophylaxis of falciparum malaria.

However, the world of FDCs is rather fraught with dangers of irrational combinations that have serious repercussions for quality, safety, efficacy and cost. Most FDCs are devoid of any rationale for combining two or more APIs (for example, more than one analgesic). It is often found that one of the APIs in the FDCs may be superfluous or wasteful as in the case of combination of vitamins with iron. Rather than enabling cost reduction, FDCs often end up increasing the cost to the patient if unnecessary APIs are combined, such as in the case of FDCs that include ibuprofen + paracetamol + caffeine. The incidence of adverse drug reactions appears to increase when combination products are administered to patients (in this case, the FDC of more than one analgesic). The inadequacy of individual APIs in FDCs is also observed in several instances, such as in the category of multivitamins. In FDCs, the prospect of identifying which API has caused adverse reactions is difficult.

The most widely prescribed FDCs that do not have a rational basis are found largely among analgesics, multivitamin preparations, cold and cough mixtures, painkillers often combined with caffeine, tonics containing incorrect proportions of vitamins and minerals, FDCs of nimesulide with other drugs, etc.

Table 6.1

Magnitude of Fixed Dose Combinations in Indian Pharmaceutical Market, 2008

Supergroup of Medicine	*Value of Single/Plain Molecules (₹ crore, 2008)*	*Value of FDCs (₹ crore, 2008)*	*Total Market of Supergroup (₹ crore, 2008)*	*FDC as Share of Total (%)*
Anti-diabetic	1,134	653	1,787	36.54
Anti-infective	4,817	1,293	6,110	21.16
Cardiac	2,266	1,152	3,418	33.70
Gastrointestinal	2,071	1,578	3,649	43.24
CNS	1,700	156	1,856	8.41
Analgesic	1,962	1,028	2,990	34.38
Respiratory	896	2,109	3,005	70.18
Blood forming	143	185	328	56.40
Dermatology	1,249	589	1,838	32.05
Gynaec	1,485	485	1,970	24.62
Ophthalmologics/otologicals	365	183	548	33.39
Vitamins/minerals/nutrients	1,681	997	2,678	37.23

Source: Authors' calculation from IMS Health, 2008.

It can be observed that the number of essential drugs on WHO EDL and national EDL within a therapeutic category is limited. These lists are mostly comprised of singly API formulations. In the private market however, a large number of formulations are available within each therapeutic segment and the number of FDCs being marketed is often more than the number of single API formulations. For example, within the therapeutic category of gastrointestinal medicines, national EDL has only 11 medicines, whereas in the open market, 45 single API-based drugs and 75 FDCs were being marketed in 2008. If dosage forms like tablets, capsules and syrups are included, the number would be several times higher. Moreover, if formulations available across various brands or manufacturers are included, the number of FDCs within this category may reach hundreds. It is also evident that the market share of these FDCs is significantly large and most FDCs are top-selling brands (see Table 6.1).

Ineffective Medicines and Medicines with Doubtful Efficacy

Besides banned/bannable drugs and FDCs which are considered non-essentials, several medicines are produced and sold which have little or no therapeutic value and therefore no clinically proven evidence exists about their efficacy. Such medicines may or may not have adverse side-effects but their use may at the most provide symptomatic relief but not clinical efficacy. Excessive and unnecessary use of multivitamin preparations or tonics is an example of this prescribing pattern. For instance, appetite stimulants (such as cyproheptadine and buclizine HCl) are not expected to be prescribed for children, since overdosage may produce hallucinations, CNS depression, convulsions and even death. Digestants, which are prescribed to boost digestion, contain concentrations of amylase, papain, persin or pancreatin and are generally not suitable in an acidic medium.

Magnitude and Pattern of Non-Essential Medicine Production and Use in India

India continues to be the leader in producing irrational medicine and therefore its use is rampant. With over 90,000 formulation packs and associated brands, the country is not only the top generics producer but a significant share of it is irrational and dangerous. Several banned, bannable and hazardous drugs float in the market unchecked. Ten of the top 25 products sold in India in 1991 and 8 of the top 25 drugs sold in 2008 belonged to one of these categories—blood tonic, cough expectorant, nutrients, liver drug, sex stimulants, etc.—which are either inessential or irrational (see Table 6.2). This also includes several fixed dose combinations that are considered inessential.

Several banned drugs and FDCs continue to thrive in the market. Despite the ban, about 46 FDCs continue to be marketed in India. Drug makers conveniently circumvent regulatory procedures to receive from state drug controllers formal marketing licences which are not approved by the Drugs Controller General of India (DCGI). According to the DCGI's own estimates, this works out to about 1,067 FDCs recently. According to the Drugs and Cosmetics Act, 1940, while the DCGI is entrusted with the function of

providing drug licensing approval for marketing of drugs, the state drug controllers are required to only approve manufacturing and selling licences of drugs in their respective states.

Table 6.2

Emerging Trends and Patterns of Inessential Medicines, 1991 and 2008 (Top 25 Brands Sold in India)

Brand	*Sales in 1991 (₹ crore)*	*Description*	*Brand*	*Sales in 2008 (₹ crore)*	*Description*
Septran	22.43	EDL	Corex	161.07	Non-EDL
Becosules	21.44	Non-EDL	Phensedyl	119.36	Non-EDL
Dexorange Plus	20.33	EDL	Human Mixtard	116.46	EDL
Rcinex	17.44	EDL	Dexorange	90.30	EDL
Brufen	16.31	EDL	Becosules	86.68	Non-EDL
Roscillin	15.41	EDL	Combiflam	74.44	Non-EDL
Norflox	14.92	EDL	Spasmo-Proxyvon	73.57	Non-EDL
Zinetac	14.84	EDL	Rabipur	68.47	EDL
Althrocin	13.43	EDL	Omez	62.46	EDL
Benadryl	13.10	Non-EDL	MT Pill	61.89	EDL
Bactrim	12.48	EDL	Zifi	60.24	EDL
Rabipur	12.31	EDL	Eptoin	59.72	EDL
Phensedyl	11.83	Non-EDL	Nise	56.31	Non-EDL
Revital	11.76	Non-EDL	Manforce	55.36	Non-EDL
Combiflam	11.29	Non-EDL	Monocef	53.17	EDL
Soframycin	11.04	EDL	Shelcal	52.95	EDL
Betnovate-N	11.01	EDL	Losar-H	52.80	EDL
Neurobion	10.64	Non-EDL	Taxim	51.17	EDL
Baralgan	10.45	Non-EDL	Revital	50.14	Non-EDL
Cobadex Forte	10.27	Non-EDL	Betnovate-N	48.20	EDL
Electral	9.60	EDL	Voveran	48.14	EDL
Trinergic B	9.31	EDL	Cifran	46.66	EDL
Cifran	9.25	EDL	Zinetac	45.94	EDL
Entero Quinol	9.21	Non-EDL	Taxim-O	45.93	EDL
Hepatoglobine	9.17	Non-EDL	Aciloc	45.91	EDL
Value of top 25 brands	329.28		Value of top 25 brands	1,687.36	
Total market value	3,675.23		Total market value	34,118.34	

Source: Authors' estimate from IMS-ORG, respective years

Changing Drug Consumption Profile in India

Table 6.3 provides a profile of the changing pattern of drug consumption between 1991 and 2008. Firstly, the period between 1991 and 2008 witnessed a 10-fold rise in medicine consumption from ₹ 3,675crore to ₹ 34,118 crore. Secondly, the consumption profile of medicines does not reflect the disease profile of the country. And thirdly, there has been a rapid increase in the range of drugs such as cardiovascular drugs, hormones, anti-diabetic drugs and nutraceuticals in the last few years. The increasing market share of such drugs partly reflects the growing burden of lifestyle diseases, especially diabetes and cardiovascular disease.

Table 6.3

Changing Drug Consumption Profile in India, 1991 and 2008

Therapeutic Category	*1991*		*2008*	
	Value of Drugs (₹ crore)	*Percentage*	*Value of Drugs (₹ crore)*	*Percentage*
Analgesics	340.18	9.26	2,990.28	8.76
Anti-diabetics	43.51	1.18	1,787.18	5.24
Anti-infectives	882.64	24.02	6,109.57	17.91
Anti-malarials	25.57	0.70	255.06	0.75
Anti-parasitic	79.33	2.16	225.94	0.66
Anti-tuberculosis	117.69	3.20	302.92	0.89
Blood-related	20.99	0.57	328.08	0.96
Cardiovascular	141.43	3.85	3,799.21	11.14
CNS	123.35	3.36	1,856.49	5.44
Dermatology	212.91	5.79	1,838.50	5.39
Gastroenterology	402.47	10.95	3,648.92	10.69
Gynaecology	203.13	5.53	1,969.70	5.77
Hepatoprotectives	33.14	0.90	359.92	1.05
HIV/AIDS	2.40	0.07	119.12	0.35
Hormone	85.45	2.32	607.77	1.78
Ophthal/Otologicals	53.96	1.47	548.27	1.61
Parenteral	27.69	0.75	152.14	0.45
Respiratory	359.53	9.78	3,005.38	8.81
Sex stimulants	32.58	0.89	307.69	0.90
Stomatologicals	3.98	0.11	194.06	0.57
Vaccine	24.19	0.66	276.28	0.81
Vitamins/nutrients	412.12	11.21	2,677.99	7.85
Others	46.97	1.28	757.87	2.22
Total	3,675.23	100.00	34,118.34	100.00

Source: Estimated from ORG/IMS Health Data Sets, respective years

Antibiotics and anti-bacterial formulations account for nearly 18 per cent of the pharmaceutical market, clearly demonstrating the huge supply-driven demand created by pharmaceutical companies. The recent controversies related to high levels of antibiotic resistance in India are a clear reflection of this induced demand. Currently, over 11 per cent of all drugs sold in the market are cardiovascular drugs, as against less than 4 per cent in 1991. Apart from a rising disease burden, this may also, in part, reflect a supply-induced demand. Anti-diabetics also witnessed a sharp increase in market share, from 1.18 per cent in 1991 to 5.24 per cent in 2008. On the other hand, the market share for tuberculosis drugs declined considerably, from 3.20 per cent to 0.89 per cent. Part of the reason could be the strengthening of the anti-TB government programme through the DOTS TB control strategy.

The large-scale promotion of non-essential drugs by the pharmaceutical industry has resulted in physicians and pharmacists in both private and public health facilities being incentivised to prescribe and dispense drugs that are irrational. Irrational practices in the prescription and dispensing of drugs continue to be rampant in the country, and are largely observed through the number of injections and antibiotics prescribed, prescriptions by brand names rather than generic names, polypharmacy and related practices. Standard Treatment Guidelines are rarely adhered to.

Irrational Drug Use in India

The WHO manual on investigation of drug use in health facilities has suggested certain indicators that could be used in research studies describing current treatment practices, comparing performance of individual facilities, monitoring and supervising drug-prescribing behaviour and assessing the impact of interventions. The following are the core drug use indicators:

Prescribing indicators:

- Average number of drugs per encounter.
- Percentage of drugs prescribed by generic name.
- Percentage of encounters with an antibiotic prescribed.

- Percentage of encounters with an injection prescribed.
- Percentage of drugs prescribed from essential drug list or formulary.

Patient care indicators:

- Average consultation time.
- Average dispensing time.
- Percentage of drugs actually dispensed.
- Percentage of drugs adequately labelled.
- Patient's knowledge of correct dosage.

Facility indicators:

- Availability of a copy of essential drug list or formulary.
- Availability of key drugs.
- Availability of Standard Treatment Guidelines.

Several studies have documented rational/irrational drug use patterns using these standard core indicators. An examination of the literature shows that poor prescribing practice which ultimately limits access to essential medicines is an omnipresent problem in India. In a study conducted by Patel *et al.* (2005), a majority of patients (80.7%) received more than one medicine per prescription. Also, non-allopathic medicines were used in 8.7 per cent of prescriptions and injectables in 5.3 per cent of prescriptions. The burden of irrational prescription was further compounded by branded medicines in 96.6 per cent of prescriptions.

A study by Kshirsagar *et al.* (1998) revealed lack of rational prescribing practices as evident in poor prescription of essential drugs (less than 60%), prescriptions dominated by fixed dose combinations and approximately 30 per cent irrational prescriptions. Bhatnagar *et al.* (2003) identified 63.33 per cent of prescriptions to be irrational, 43.33 per cent prescriptions with at least one antibiotic and 10 per cent prescriptions with injectables. Yet another study, conducted by Bhartiy *et al.* (2008), highlighted similar findings where the proportion of drugs from EDL was 66.9

per cent, with a high number of prescriptions with antibiotics (60.9%) and injections (13.6%).

Although the findings are similar in respect to poor prescription practices, the contextual background of these studies is different—they are from different states of the country with different primary units as samples. Patel *et al.* focused more on private practitioners and on quality of prescriptions in terms of clarity and adequacy of the information to describe the types and number of medicines prescribed. In a similar but rather detailed study conducted by Kumari *et al.,* 2008, the evil of polypharmacy was apparent (3.1 drugs per prescription), while prescriptions with generic names constituted only 27.1 per cent. The prescriptions at the secondary-level health facilities were incomplete with respect to mention of the suffix/prefix of the drug, full name, dose, frequency and strength of the drug, and directions specifying the route and duration of the treatment. The average cost of drugs/prescription/day (mean, standard deviation) was found to be the highest at the tertiary level ($0.34, 0.43), decreasing significantly at the primary-level health facilities. The analysis by Kshirsagar *et al.* was quite comprehensive in terms of parameters but was limited to a district; the findings of Bhartiy *et al.* were from public health facilities but, as with previous studies, were limited to a district.

Analysis of Prescription Practices

This section[2] is devoted to understanding the prescription behaviour of physicians in public health facilities in the states of Bihar and Tamil Nadu. As far as the sample design was concerned, the survey was conducted in 17 districts of Bihar and 18 districts of Tamil Nadu covering 60 health facilities, 30 community health centres in each state. Approximately 20-30 prescriptions were collected per facility, with a total sample size of close to 1,200-1,500 prescriptions. However, final analysis was conducted only on 1,227 prescriptions (Bihar 733, Tamil Nadu 494) as many did not fulfil the selection criteria. [These included poor-quality prescriptions (writing not legible, drug name, dose and duration not mentioned,

2. This section draws heavily from Selvaraj *et al.* (2011).

etc.) which thus had to be dropped from the analysis.] The total number of drugs analysed on the prescriptions was 3,444, with a break-up of 1,922 from Bihar and 1,522 from Tamil Nadu.

Among the core prescription indicators, one of the most useful and robust is the average number of drugs per encounter, which measures the extent of polypharmacy. The range was from one to five drugs per prescription for both Bihar and Tamil Nadu; however, the average for Tamil Nadu was higher, at 3.1 drugs per prescription, as compared to 2.6 for Bihar (Table 6.4). Polypharmacy is considered a poor prescribing practice which may have many underlying causes ranging from prescribers' training needs to health system issues of poor governance and accountability. .

Table 6.4 highlights the fact that the percentage of drugs prescribed by generic names was 73.5 per cent for Bihar as compared to 88 per cent for Tamil Nadu. However, the percentage of drugs prescribed from the EDL shows a sharp decline for Bihar to 66.8 per cent as compared to Tamil Nadu's 88 per cent. Ideally the figure for drug prescriptionsby generic name and from the EDL should be close to 100 per cent as these indicators are surrogate measures for understanding how much the practice conforms to national guidelines and policies. In our study, a 90 per cent cut-off is also acceptable since 90 per cent of all drugs procured at the state level (in Tamil Nadu) are from the EDL.

Table 6.4

Select Prescription Indicators in Bihar and Tamil Nadu

	Bihar	*Tamil Nadu*
Average number of drugs per encounter	2.6	3.1
Percentage of drugs prescribed by generic name	73.5	88.0
Percentage of drugs prescribed from Essential Drug List	66.8	88.0
Percentage of encounters with an antibiotic prescribed	66.0	59.6
Percentage of encounters with an injection prescribed	4.9	1.4
Percentage of fixed dose combinations versus single agents	6.9	0.0
Percentage of encounters with a syrup prescribed	26.2	2.6

The core indicators on the percentage of encounters with at least an antibiotic and an injection prescribed measure practices for two costly and commonly overused medicines. The figures for encounters with an antibiotic and an injection for Bihar were 66.0 per cent and 4.9 per cent respectively, certainly on the higher side as compared to Tamil Nadu with 59.6 per cent and 1.4 per cent. There is a positive relationship between polypharmacy and the increased number of antibiotics and injections prescribed. Recent studies have identified poor prescription practices as one of the factors for emerging drug resistance.

Table 6.5

Distribution of Prescription Medicines

Prescription Indicator	*Bihar*	*Tamil Nadu*
Generic drugs	73.5	88.0
EDL drugs	66.8	88.0
Antibiotics	29.8	23.1
Fixed dose combinations	6.9	0.0
Injections	3.1	0.9
Syrups	12.5	1.4

Further, the study findings suggest that the proportion of antibiotics[3] out of all prescribed medicines was 29.8 per cent and 23.1 per cent for Bihar and Tamil Nadu respectively (Table 6.5). The figures for injections[4] stood at 3.1 per cent for Bihar and 0.9 per cent for Tamil Nadu.

The percentage of FDCs prescribed was 6.9 per cent in Bihar whereas it was 0 per cent in Tamil Nadu. FDCs have a limited role in routine therapeutic management and are rather notorious for adverse reactions. Similarly, syrups (cough syrups, vitamin supplements and nutrition supplements) have dubious therapeutic efficacy. The percentage of encounters with syrups prescribed was

3. The term antibiotic is exclusive of following therapeutic class of medicines, i.e. anti-fungals, anti-helminthics, anti-amoebics, anti-scabies preparations, topical antibiotics and antibiotic ear/eye drops preparations.

4. The injection includes antibiotic injections, Anti-Rabies Vaccine, Tetanus Toxoid and is exclusive of injections for immunisation.

26.2 per cent for Bihar as compared to a paltry 2.6 per cent for Tamil Nadu.

Table 6.6a

Number of Drugs per Prescription by Core Indicators: Total, Generics, EDL Drugs

Drugs per Prescription	*Proportion of Prescriptions*		*Prescriptions of Generic Drugs*		*Prescriptions of Drugs from the EDL*	
	Bihar	*Tamil Nadu*	*Bihar*	*Tamil Nadu*	*Bihar*	*Tamil Nadu*
0	0.0	0.0	6.0	0.8	10.5	0.8
1	7.5	1.8	28.1	7.7	30.0	7.9
2	39.2	19.9	37.5	30.5	36.0	30.5
3	38.9	52.2	24.3	44.1	20.7	43.7
4	12.6	19.3	3.8	13.0	2.7	13.2
5	1.9	6.5	0.3	3.9	0.0	3.9
Total	100.0	100.0	100.0	100.0	100.0	100.0

As evident in Table 6.6a, the prescription analysis also reveals that some 78 per cent of prescriptions from Bihar had either two or three drugs on them, as compared to around 72 per cent for Tamil Nadu. The proportion of prescriptions without even a single generic drug and EDL drug was 6 per cent and 10.5 per cent respectively for Bihar, as compared to 0.8 per cent and 0.8 per cent for Tamil Nadu. This distortion could be due to poor procurement practices in Bihar leading to unavailability of essential medicines, forcing poor prescriptions.

Table 6.6b

Number of Drugs per Prescription by Core Indicators: Antibiotics, FDCs, Injections, Syrups

Drugs per Prescription	*Prescriptions of Antibiotics*		*Prescriptions of FDCs*		*Prescriptions of Injections*		*Prescriptions of Syrups*	
	Bihar	*Tamil Nadu*	*Bihar*	*Tamil Nadu*	*Bihar*	*Tamil Nadu*	*Bihar*	*Tamil Nadu*
0	28.1	34.8	82.3	100.0	93.6	98.0	70.9	96.5
1	66.0	59.6	17.5	0.0	4.9	1.4	26.2	2.6
2	5.5	5.1	0.3	0.0	1.4	0.6	2.1	0.8
3	0.4	0.6	0.0	0.0	0.1	0.0	0.7	0.0
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

The proportion of prescriptions with at least an antibiotic was 66.0 per cent, one FDC was 17.5 per cent, one injectable was 4.9 per cent and syrup was 26.2 per cent for Bihar, while the indicators for Tamil Nadu were considerably better with just 1.4 per cent of prescriptions with injections, 2.6 per cent of prescriptions with syrups and none with FDCs (see Table 6.6b).

Table 6.7

Relative Change in Distribution of Core Indicators with Drugs per Prescription

Drugs per Prescription	*Generic Drugs*	*EDL Drugs*	*Antibiotics*	*Syrups*	*Injections*	*FDCs*
			Bihar			
1	80.0	67.3	23.6	7.3	14.5	1.8
2	75.4	66.7	31.9	12.0	3.8	6.8
3	76.0	69.9	30.5	13.0	1.6	7.4
4	65.2	62.0	26.6	13.9	4.1	6.5
5	64.3	54.3	25.7	8.6	1.4	7.1
			Tamil Nadu			
1	66.7	77.8	11.1	11.1	0.0	0.0
2	87.2	87.2	26.5	1.0	0.5	0.0
3	89.5	89.1	23.3	1.2	0.3	0.0
4	86.1	86.3	22.4	1.3	1.1	0.0
5	89.4	89.4	21.3	2.5	3.8	0.0

Further, a detailed analysis conducted to estimate the proportionate rise in the number of antibiotics, injectables, FDCs and syrups with increase in the number of drugs per prescription revealed that there is a positive relationship. Also, the relationship is more perceptible in Bihar as compared to Tamil Nadu. As the number of drugs per prescription increases, the proportions of drugs with generic name and EDL drugs decrease on account of increase in prescription of syrups, FDCs and injectables. The relationship with antibiotics is balanced, with not much rise or fall, probably because of their essentiality for the patient. However, no such relationship was discernible in Tamil Nadu, except for injectables, as the shares of drugs with generic names, EDL drugs and antibiotics remained proportionate irrespective of increase in number of drugs per prescription (see Table 6.7).

As evident from the core indicators listed above, drugs prescribed by generic name and from the EDL were low in Bihar and were compensated by non-EDL drugs. To estimate and ascertain whether the non-availability of EDL drugs had an impact on access to medicine, further analysis of prescriptions as per drugs across various therapeutic categories was conducted (Table 6.8). The scrutiny reveals that the drugs most frequently prescribed and dispensed at public health facilities in Bihar were anti-bacterials (22.4%) followed by analgesics/antipyretics (19.9%), which is contrary to conventional prescribing norms. At community health centres, since microbiologic diagnosis is rarely undertaken and drugs are prescribed to relieve symptoms, higher proportion of antibiotic prescriptions should be discouraged. Also, prescriptions of vitamins and minerals which have dubious pharmacological value were common (10.7%) in Bihar. Similarly, prescriptions of anti-asthmatics, which include cough syrups, were on the higher side (10.3%).

Table 6.8

Distribution of Prescription Medicines across Therapeutic Categories

Therapeutic Category	*Bihar*	*Tamil Nadu*
Analgesic/Antipyretic/NSAID	19.9	24.2
Anti-bacterial	22.4	20.5
Anti-allergic	6.6	14.9
Vitamins and minerals	10.7	12.2
Anti-asthmatic	10.3	1.4
Antacid	4.5	5.3
Anti-amoebic	2.8	3.2
Anthelmintic	2.7	0.7
Anti-fungal	1.9	0.7
Anti-spasmodic	1.3	0.9
Anti-anaemic	2.9	0.0
Anti-emetic	0.3	0.9
ORS	1.0	1.2
Anti-hypertensive	0.0	3.4
Anti-diabetic	0.0	1.3

However, in Tamil Nadu the major drugs prescribed were analgesics/antipyretics (24.2%) followed by anti-bacterials (20.5%). The prescription pattern for vitamins and minerals (12.2%) was similar to Bihar's, but here the major class of drugs prescribed for respiratory illness was anti-allergics (14.9%) not anti-asthmatics (1.4%). Also, the prescriptions with drugs for chronic diseases like hypertension (3.4%) and diabetes (1.3%) in Tamil Nadu can be considered a positive health system response. The prescription of anti-fungals, anthelminticsand anti-anaemics was low as compared to Bihar.

An interesting observation concerns respiratory system medicines. Bihar's public health facilities often prescribe cough syrups (anti-asthmatics), which have inconclusive pharmacological benefits in terms of effectiveness, whereas in Tamil Nadu, rational prescription with anti-allergics was made. There were no prescriptions with drugs for diabetes and hypertension in Bihar, suggesting poor prescriptions. The major drugs prescribed in both states were analgesics/antipyretics and anti-bacterials, and further analysis of these therapeutic classes by individual drugs revealed that in Bihar the range was large, extending from generics to branded versions, EDL to non-EDL, single agent to FDCs, oral, injectables, etc.

Summing Up

Production of inessential and irrational medicines is very common in India. Their prescription, dispensing and use are equally rampant as drug makers succeed in their strategy to push these medicines through their promotional machines. Several banned and bannable drugs continue to thrive in the Indian pharmaceutical market, which is also flooded with unnecessary and irrational FDC drugs across all therapeutic categories. Although the market has witnessed considerable growth and change in the last 20 years, the change and the composition of the market do not reflect the epidemiological profile of the country.

In India, at the central level, three ministries are responsible for regulation of the health and pharmaceutical sectors—the Ministry of Health and Family Welfare (MoHFW), the Ministry of Commerce

and Industry, and the Ministry of Chemicals and Fertilisers (through the Department of Pharmaceuticals and its National Pharmaceutical Pricing Authority). The Drugs Controller General of India (DCGI) under the MoHFW is responsible for licensing and standards. The federal authorities are responsible for approval of new drugs, provision of standards, quality control over imported drugs, coordination of the activities of state drug control organisations, and providing advice to allow for uniformity in enforcement of the Drugs and Cosmetics Act.

Under the Act, regulation of the manufacture, sale and distribution of drugs is primarily the concern of the state rather than federal authorities. The responsibility for Indian drug regulation is therefore divided between the central and state governments. Each of the 28 states has its own drug control organisation that is responsible for drug quality and a system of licensing for the manufacture, sale and distribution of drugs within that state. The central government is supposed to coordinate the activities of individual states. Schedule M of the Drugs and Cosmetics Act lays down the Good Manufacturing Practices (GMP) that manufacturers are required to follow to ensure consistent quality standards. Schedule M was amended in December 2001 to upgrade the requirements to WHO GMP standards.

There has been an alarming increase in irrational FDC drugs in the recent past and the pharmaceutical companies manufacturing these drugs are luring physicians to prescribe their products even when they are unnecessary for the patients. As per the Drugs and Cosmetics Act and Rules, the Central Drug Standard Control Organisation is responsible for granting approval for "new drugs". FDC drugs which are new in India are also considered as "new drugs" as per Rule 122E of the Drugs and Cosmetics Rules as included in 1999.

It would be pertinent to highlight that the DCGI has taken cognisance of the flooding of the market with irrational FDC drugs and directed all state drug controllers to take necessary action with respect to FDCs in the year 2007.[5] It included the list of more than

5. vide letter no. F.No. 19013A/2007-D dated 14 August 2007

1,000 FDC drugs not permitted by the DCGI but permitted by state drug regulators. In September 2007, the DCGI had circulated a notification declaring 294 FDC drugs as irrational. However, the Confederation of Indian Pharmaceutical Industries (CIPI) moved the Madras High Court and received a stay order on the DCGI's directive against the 294 FDC drugs categorised into "absurd", "rejected", "banned", and "under examination". Interestingly, the CIPI was willing to withdraw the cases if the DCGI agreed to allow licences to the 150 FDC drugs which were categorised as "need[ing] further examination". The present DCGI list of unapproved FDC drugs contains 115 combinations.

Poor prescription practices leading to higher proportions of antibiotics, injectables, FDC drugs and syrups in prescriptions may have to do with prescribers' lack of training in rational drug use, coupled with strong promotion and marketing of branded and non-EDL drugs, and financial incentives for polypharmacy.

In addition, there may be pressure from the patient's side because of cultural beliefs, expectations and demands. For instance, a visit to public health facilities suggests that cough syrup is often demanded by the patient irrespective of his or her prevailing health condition. This shows contextual underpinnings in irrational prescriptions and use because of unavailability of essential medicines, poor diagnostic facilities, weak regulation and lack of epidemiological basis for decision-making.

The emerging evidence points towards the need for capacity-building of health professionals in rational drug use and implementation of Standard Treatment Guidelines at the facility level to improve patient outcomes, rationalise medicine prescriptions and reduce costs.

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7

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Recent Trends in India's Pharmaceutical Innovation

Introduction

Innovation in India's pharmaceutical sector assumes critical importance, especially in the post-TRIPS (Trade-Related Aspects of Intellectual Property Rights) scenario, because of various claims made by the proponents of the new patent system in the pre-TRIPS period. This chapter examines various facets of post-TRIPS scenario drawing evidence from the current trends and pattern of emerging innovation in India.

Two perspectives emerge on the impact of the policies on innovation for sustainable development of the Indian pharmaceutical industry. The first shows how the prospects of industrial competitiveness are getting influenced by the adoption of stronger patent system and external liberalisation. This perspective, articulated by Athreye *et al.* (2008) and Arora *et al.* (2008), starts implicitly with a highly optimistic predisposition with regard to the domestic patent reform and external liberalisation. In their view, both patent reform and external liberalisation were necessary in the long run to put the industry on the path of radical pharmaceutical innovation. In their view, these reforms have already successfully produced a significant process of creative destruction. This perspective does not go into the question of who has benefited from the gains that the country has been able to make from the advancement of innovation in the pharmaceutical sector in India, but focuses on the assessment of the industry's strategy where

firm-specific deployment of capabilities, entrepreneurship and *ad hoc* problem solving skills determine the winners of the race for market shares, as new or untapped economic opportunities emerge.

The second perspective argues that not all problems of development in third world countries can be solved by strengthening policies that encourage competitiveness of the industry alone, which are mainly economic in nature, but these policies may only be instrumental and acceptable, if so designed, in promoting sustainable development in the social, environmental and political spheres. In this perspective, for competitiveness policies to play this role, developing countries must actively pursue sustainable development goals, and not just increasing exports. Corrales-Leal (2007) argued in favour of the measures that must be taken to develop local capabilities to permanently differentiate and diversify production, and to increasingly enhance productivity and add value to exports.

As the adherents of this perspective are yet to undertake a detailed evaluation of the contribution of the Indian pharmaceutical sector to industrial development and public health, they have some broad suggestions to offer in terms of strengthening public sector, getting the government to enhance investment in public health and preventing brown-field foreign direct investment (FDI). This approach has been largely reflected in the works of Abrol (2004), Dhar and Gopa Kumar (2006) and Chaudhuri (2005). Within this perspective, assessments undertaken of the post-TRIPs performance of pharmaceutical industry demonstrated that there are costs associated with product patent protection, and these costs may also soon extend even beyond the adverse impact on prices of essential medicines.

In this contribution, using an industry-wide innovation metrics, we assess firm level in-house research & development (R&D) activity of pharmaceutical firms and public sector science system. Evidence is provided on the nature of contribution of technology transfer and overseas R&D of foreign firms. We also assess the role played by the post-TRIPS drug innovation promotion initiatives of the Government of India (GoI) while innovation metrics focus on the disease orientation and stage of development of R&D outcomes

resulting from the investment activity of the domestic and foreign pharmaceutical firms operating from India. We also appraise the prospects of development of new pharmaceutical products in the context of emerging challenge of double disease burden in India

Assessment of Post-TRIPS Innovation Routes

The post-TRIPS innovation policy was formulated as the advocates of TRIPS Agreement claimed that India would be attracting high quality FDI, technology transfer and overseas R&D in the field of drug innovation. Based on this expectation, the policy makers were upbeat about the prospects of Indian pharmaceutical industry and its potential contribution to the processes of drug innovation. Although evidence now exists about the loss of welfare and wealth as a consequence of the implementation of TRIPS Agreement, yet when it came to India, their conclusion was quite positive about the likely impact of TRIPS on drug innovation. Lall and Albaladejo (2002) assessed the case for uniform and strong intellectual property rights (IPRs) for developing countries as a whole by classifying them using various measures of domestic innovation and technology imports. His analysis suggests that it is possible to argue that India has now reached a stage in pharmaceutical production where stronger IPRs would induce greater innovation by local firms, though the benefits of which would have to be set off against the closure of other firms.

The proponents of TRIPS Agreement have also been following up on the idea of the route of global integration of pharmaceutical industry to make a case for upgrading the innovation system in view of TRIPS. For example, Lanjouw (1998) notes that for an Indian firm taking the first steps towards new molecule discovery, the ability to lower costs by sub-contracting or by joining with foreign firms in research joint ventures is particularly important. Even limited R&D and pharmaceutical production taking place now through the expansion of pharmaceutical production and sales is knowledge-intensive and has some impact. Both, generics as well as patented products tap into learning, and they are both increasingly responsible for expanding markets in the pharmaceutical sector (Granville and Leonard, 2003).

But thanks to the astute vigilance of the coalition of social movements and domestic pharmaceutical industry, the policymakers tackled the challenge of TRIPS by delaying the policy of external liberalisation and the postponement of implementation of product until 2005. Of course, all these policy debates were taking place in the midst of strong opposition put up by global pharmaceutical firms and neo-liberal group in the political and bureaucratic apparatus.

TRIPS Implementation, FDI, Technology Licensing and R&D

Although the opponents of TRIPS were focusing on the challenges of access to medicine and protection of domestic market, for the policy makers the prospects of getting significant access to export market was a priority. While accepting the membership of World Trade Organization (WTO), the government claimed that the TRIPS Agreement had sufficient remedies. Assurances were given that the Indian government would continue to monitor and remedy the adverse impact of the implementation of TRIPS on access to medicine.

However, to what extent the TRIPS agreement would offer an advantage in respect to incentivisation of technology transfer, investment in manufacturing and R&D was not rigorously debated. The major challenge of how the government will deal with the issue of access to medicines remained a dominant concern with public interest groups. As there was not much discussion on the kind of learning, competence building and innovation that would be encouraged in case the country chooses to focus mainly on the opportunity available in the regulated markets, the issue of innovation which relates far more to the problem of access to future medicine did not occupy much attention in the debate.

But we are now in position to take a deeper view based on empirics. Below we analyse the evidence of the gains that would accrue on relying largely on FDI, technology transfer and R&D investment from overseas, by assessing in detail the activities of the sample firms listed in Table 7.1.

Table 7.1

Sample Characteristics of Selected Pharmaceutical Companies

Total Number of Listed Companies in Prowess Database	*Number of Selected Companies in the Sample*	*Total Sales (in crore)*	*Total Sales of selected Companies (in crore)*	*Percentage*
134	(Domestic + foreign) 50	55,214.06	50,397.46	91.27
134	(Domestic) 41	55,214.06	39,745.47	71.98
134	(Foreign) 9	55,214.06	10,651.99	19.29

Source: CMIE Prowess Database, 2009, URL, *www.cmie.com.*

Analysis of Activity-wise FDI

Table 7.2 shows that recently research and development activity has accounted for the highest number of projects with a total of 36, representing 43 per cent of investment projects, but as far as the quality of FDI being received is concerned, evidence may be misleading.

Table 7.2

Industry Analysis: Number of FDI Projects by Activity

Business Activity	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*Total*	*Average Annual Growth*
R&D	2	4	10	5	8	5	2	36	44.5%
Manufacturing	3	8	6	3	3	5		28	n/a
Sales, marketing and support		2	2	3	1	1	1	10	n/a
Design, development and testing		1	1		2	1		5	n/a
Business services			1					1	n/a
Headquarters				1				1	n/a
Logistics, distribution and transportation					1			1	n/a
Retail		1						1	n/a
Total	5	16	20	12	15	12	3	83	42.0%

Source: FDI Markets Intelligence, URL *www.fdimarkets.com.*

Our analysis shows that a large number of foreign R&D investment projects are focused on the development of facilities for

phase III clinical trials and other such modules that only integrate the Indian talent and facilities into the global objectives of foreign pharmaceutical firms. As such, these R&D projects have little to do with the needs of local population. Thus, the quality of FDI being attracted into pharmaceutical R&D cannot be characterised as really high.

Overseas R&D

It is evident that the agreement on TRIPs has not succeeded in inducing the foreign firms to take up overseas R&D for the discovery and development of drugs where the Indian markets could be large. In cases where multinational companies (MNCs) had located part of their global R&D outfit to India, activities have been declining. While Barring Hoechest and Astra are involved in limited drug discovery, others have closed down the units that had the mandate to develop products for the local markets. Earlier Ciba-Geigy had a larger presence in R&D; its R&D centre is now closed in India. Hoechest has also been reducing its involvement in R&D in India. Their current strategy is to reduce the locally oriented in-house R&D investment in India. They are now building on the work done at these centres on natural products in European laboratories.

There is also evidence that R&D activities of MNC subsidiaries reflect more thrust on formulation R&D (or product development) compared to bulk drug R&D related process development. Their focus remains on conventional dosage forms. Although few of them manufacture novel drug delivery system (NDDS), no research on NDDS is being undertaken at the subsidiaries. Table 7.3 provides details of contribution made to the pattern of innovative activities undertaken for the domestic market by foreign pharmaceutical firms from the Indian soil.

Table 7.3

Directions of Innovative Activities of Foreign Firms, 1999-2009

Foreign Company	*CMIE Rank*	*Compounds Commercia-lised*	*Process Patents*	*NDDS*	*NCE*	*MOT*	*New Forms of Substances*	*Other Products*
1 Ranbaxy Laboratories	3	71	88	20		4	109	239
2 GSK Pharmaceutical	8	4						
3 AstraZeneca Ltd.	59	4						
4 Pfizer Ltd.	28	3						
5 Shanta Biotech	137	5						
6 Novonordisk			1		2			1
7 Alfred								1
8 Hindustan Lever/Unilever			30			18	18	363
9 Johnson & Johnson								3
Total		87	119	20	2	22	127	607

Note: NDDS: novel drug delivery system; NCE: new chemical entity; MOT: Method of Treatment. Other products included skin products, cosmetics, oral dental care, toiletries products, antifungal, antibacterial, antimicrobial products. Note that until recently, Ranbaxy was a domestic firm. Pharmaceutical activities of Hindustan Levers are rather low and focus on cosmetics.

Source: Data of commercialisation and launched compound collected from news archive search of individual pharmaceutical companies from 1999 to 2009, and emerging patterns of pharmaceutical innovations (Process, product, NDDS, NCE, dosage/formulation/composition, salt/polymorphs/derivative) data collected from the United States Patent and Trademark Office (USPTO) of 1992-2007. See *http://www.uspto.gov/*.

Centre for Monitoring Indian Economy (CMIE) Rank was created according to total annual sales of the companies, year 2010-11.

Domestic Pharmaceutical Firms and Technological Capability Building

Policy makers have focused on technological capability building processes in the Indian pharmaceutical industry since early 1970s. Before the beginning of 1970s, a national system of innovation was lacking in the processes of establishment of large domestic pharmaceutical firms. The decade of 1970s is known for introducing a new process patent legislation and adopting a drug policy in 1978. The Patent Act of 1970, which did not allow product patents in the area of pharmaceuticals, was adopted to step up technological

capabilities and innovation for the development of generic industry. Under the Indian Patent Act, 1970, the country's national system of innovation was free to develop alternate processes for the drugs that were still under product patent protection (on-patent drugs) in the developed countries.

Several domestic firms came on the local market scene using the technologies for alternate processes developed in-house and by the public sector research laboratories of Council of Scientific and Industrial Research (CSIR) during the 1980s. Over 50 new processes were developed during the period 1965-1980 in the CSIR system for the benefit of Indian pharmaceutical firms. For over 100 essential drugs, the CSIR laboratories gave new processes, many of which were based on the development of new steps and involved the development of close to 50 new reactions in chemistry.

Export of Generics and Process Innovation

All big Indian companies like Ranbaxy, Cipla, Nicholas Piramal, Reddy's, Lupin, Orchid, Matrix and Wockhardt have preferred the route of generics exports to the regulated markets of the United States (US) and Europe for the realisation of potential for the firm growth and capability upgrading. These companies have been investing significant funds into the generic market with the expectation that they should be making maximum out of these markets when the market competition is low and the margins are high. As this scenario is possible only in the beginning, when the drugs become off-patent, they are filing four to five Abbreviated New Drug Application (ANDAs) every year to be the first in the market and exploit the period of exclusivity available under the US drug regulation laws.

Experience however indicates that the road ahead for the export of generics to the regulated US market is likely to be tedious and full of hurdles. From being producers of broad-range generics, Indian companies have had to learn to challenge the US patent law. But this has not been an easy task. Litigations are costly and can run into figures of US$ 15-18 million to be successful. Both Ranbaxy and DRL have already burnt a lot of money in this business. Hurdles are growing because both the US and EU are everyday

taking steps that can help the MNCs to maintain monopoly in the area of pharmaceuticals even beyond 20 years. In the US, this kind of pharmaceutical-specific re-engineering of patent length and breadth has been made possible with the involvement of US Food and Drug Administration (USFDA), the body responsible for drug regulation. The constraints of a unitary patent system have led the US to extend the period of market exclusivity for drugs by adjusting the system with the help of drug regulators. Today the generic export route is the main target for tightening of the generics legislation in the US. Indian pharmaceutical firms cannot assume the traditional pharmaceutical generics opportunity to fall on their lap. As the evidence shows, even in the area of bio-generics, a tough fight is in waiting for the Indian pharmaceutical industry.

The recombinant products market has been led so far by imports of established global brands and marketing of the products either by local subsidiaries (SmithKline Beecham, Novo) or through marketing arrangements as in the case of Nicholas Piramal and Roche. Although changes have come in due to the recent introduction of local firms, such as Shanta, Bharat, Panacea and Wockhardt in the Indian market for products like hepatitis B vaccine, interferon-alpha, insulin and erythropoietin (EPO), the situation is to change radically after January 1, 2005. As already discussed in the earlier section, the Indian policy makers should expect litigations to grow in the case of bio-generics. The Indian industry is getting a taste of this at an early stage. Almost all the export-oriented Indian firms have faced recently this challenge in the US.

Below we review the evidence built on the basis of post-TRIPS industry-wide patenting activity undertaken by all the leading Indian companies. Analysis shows that though the domestic firms are investing far more regularly in creating firm-specific competences than in the past, as far as the orientation of investment on in-house R&D of domestic pharmaceutical companies is concerned, directions of work seems to have been mainly focused on the development of capabilities, innovations and technological know-how for off-patent generics that the industry thought could be exported to regulated markets of Europe and the US. See Table 7.4 for the historical timeline of capability development profile

mapped by the authors on the basis of patents filed by the Indian pharmaceutical industry with the USPTO.

Table 7.4

Emerging Patterns of Pharmaceutical Innovations, 1992-2007

No.	*Nature of Patent*	*1992-1995*	*1996-1999*	*2000-2003*	*2004-2007*	*Total*
1	Process patent	1	8	62	149	220
2	Product patent		6	18	38	62
3	NDDS patent			11	20	31
4	NCE patent		2	10	23	35
5	Dosage/formulation/ composition of matter patents	2	43	228	285	558
6	Method of treatment		1	19	16	36
7	New form of substance		5	85	195	285
	Total	3	65	433	726	1,227

Note: NDDS: novel drug delivery system; NCE: new chemical entity.

Source: Data on emerging pattern of patenting activity of domestic (30) and foreign (5) companies active in India (process, product, NDDS, NCE, dosage/formulation/ composition, salt/polymorphs/derivative) are collected from USPTO, 1992-2007, *www.uspto.gov/*.

Table 7.4 shows that the chemistry-driven process research leading to non-infringing processes for active pharmaceutical ingredients (APIs), introduction of cost-effective routes, identification and characterisation of impurity profiling pertaining to APIs, reduction of impurity levels, acceptable dosage forms and formulations came to be pursued as priority in the Indian pharmaceutical industry during the post-TRIPS period. And this emphasis continues to reflect till this date. The other area of R&D pertains to formulations where NDDS-based products are introduced. Our analysis also confirms that the economic opportunity created by the Hatch-Waxman Act of 1984 has been the most important stimulus for the domestic Indian pharmaceutical firms to invest in the processes of learning, competence building innovation making activity.

India is more efficient in converting APIs to finished products and is significantly ahead of China in formulation export. While it is true that China lags behind in formulation manufacturing expertise

and does not have presence in the sales of generic formulations as much as India, comparison of molecules filed from India and China reveals that India is absent in several fermentation and biotech products. India has presence in small molecular chemistry. It is mostly absent in peptides, biopharmaceuticals and biotech products. According to IMS-Health the market for fermentation technology products and other biotech products is growing at double the rate of the pharmaceutical product market. Table 7.5 provides the list of biotechnology drugs involving China's strength in molecules where India has no Drug Master Files (DMFs).

Table 7.5

List of Biotechnology Drugs Showing China's Strength in Molecules where India has no Drug Master Files (DMFs as in September 2008)

Molecule	*Total No. of DMFs*	*DMFs by China*	*Method of Production*
Acarbose	4	2	Fermentation
Bivaluridine	2	1	Fermentation
Bleomycine	4	2	Fermentation
Capreomycin	2	1	Fermentation
Clavulanic acid	15	1	Fermentation
Cyclosporine	10	3	Fermentation
Dactinomycin	2	1	Fermentation
Desmopressine	8	1	Fermentation
Floxuridine	2	1	Fermentation
Flumethasone	4	1	Fermentation
Gentamicin	3	2	Fermentation
Heparin	17	8	Extraction from animal intestine
Hydrocortisone	19	5	Fermentation
Ivermectin	2	2	Fermentation
Monoclonal antibody	27	0	Cell culture
Mupirocin	6	1	Fermentation
Prednisolone	29	4	Fermentation
Thiostrepton	1	1	Fermentation
Vancomycin	6	2	Fermentation
Various salt of penicillin	20	4	Fermentation

Source: Compiled by Abrol *et al.* (2010).

Contribution of Generics Exports to Manufacturing and Research Capability

Another major area of competence building has been related to the improvement of good manufacturing practice. Table 7.6 shows the key areas of competence building in the case of domestic pharmaceutical firms in relation to the registration of DMFs and ANDAs prior to registering products (generics) in the EU, the US and other developing countries. The new drug applications (NDAs) filed with United State Federal Drug Regulation Authority (USFDA) have still been far and few in the case of Indian pharmaceutical industry. Table 7.6 shows the firm level pattern of distribution of DMFs, ANDAs and NDAs filed by the Indian pharmaceutical companies from 1980 up to 2008.

Table 7.6

Drug Master Files, Abbreviated New Drug Applications and New Drug Applications Received by Top 15 Indian Companies, from 1980 to 2008

Company	*No. of DMFs*	*No. of ANDAs*	*No. of NDAs*	*Sales Turnover as on 2008 in CMIE Prowess Data Base (₹ crore)*
Ranbaxy Laboratories	107	241	17	11,187.58
Dr. Reddy's Laboratories	160	144	1	9,966.27
Cipla Ltd.	153	-		11,057.1
Sun Pharmaceutical	129	179		5,502.5
Lupin Ltd.	85	90		6,430.75
Cadila Health care Ltd.	76	92		4,635.9
Wockhardt Ltd.	66	67		3,678.15
Aurobindo Pharma Ltd.	128	147		5,876.04
Matrix Laboratories Ltd.	115	41		2,538.18
Glenmark Pharma	42	71	1	2,868.30
Orchid Chemicals	73	57		3,067.56
Strides Arcolab	3	na		1,487.72
Ipca Laboratories	73	na		2,929.02
Biocon Ltd.	22	na		2,519.49
Piramal Health care	10	na		5,218.57
Total (15 companies)	1,242	1,129	19	

Source: Number of DMF data from *http://www.betterchem.com* (drug master file database) and number of ANDA from individual company website, Sales Turnover—CMIE (PROWESS).

Analysis undertaken of the inventive activity shows that while the Indian pharmaceutical industry has gradually changed during the post-TRIPS period and it is now an R&D-based industrial segment which is competent to participate in the processes of learning, competence building and innovation for the supply of off-patent generics to regulated markets, in the field of product development, bulk of the 'innovative outputs' still belong to mainly the areas of dosage/formulation/composition of matter related to R&D work.

Contribution of Contract Research and Manufacturing Services (CRAMS)

However, the expected benefit of increased technology and knowledge transfer from foreign to domestic firms is yet to accrue in India. Foreign technical collaborations have not been important for export, yet many small and medium scale firms have entered into collaborations with foreign firms mostly to cater to the domestic market. Exploitation of contract manufacturing would also not be able to improve the prospects for technology transfer by itself because there are no new technologies being transferred. Analysis indicates that though players like Matrix Laboratories, Divi or Shasun Chemicals or Cadilla have made much use of this opportunity to grow, their technological capabilities have not been upgraded through the provision of contract manufacturing services. Recently USFDA warned Matrix Laboratories about their manufacturing practice. Apart from Ranbaxy and Cipla, which were earlier warned by the USFDA, Matrix was the third drug company working from India for the US market to get warning from the US regulatory authorities.[1]

There is also evidence that as far as the terms and conditions of contract manufacturing of bulk drugs are concerned, in the post-TRIPS scenario, deals being entered in to by the Indian firms are far from being equal. Ranbaxy Laboratories and Lupin Laboratories were

1. When it comes to manufacturing, India ranks only second to the US in the number of global DMF every year. DMF is essentially permission to enter the US bulk actives market with the objective of either supplying to a large US generics player or captive consumption. DMFs by Indian companies rose to 19 per cent of the world filings in 2003 compared to 2.4 per cent in 1991. For the April-June Quarter 2003, India accounted for 34 per cent of the world's filings.

among the first Indian companies to bag manufacturing contracts from multinational companies—Ranbaxy from Eli Lilly and Lupin from Cynamid. In pre-TRIPS scene, contracts for manufacturing came through when Ranbaxy developed an alternative process for manufacturing Eli Lilly's patented drug Cefaclor because the US company sensed that it would lose its markets to Ranbaxy's low-cost substitute in countries that did not recognise product patents. Eli Lilly offered a manufacturing contract to Ranbaxy for producing 7ACCA (7-amino-3-chloro-3-cephem-4-carboxylate), intermediate for Cefaclor (second generation antibiotic used to treat bacterial infections) to make the best of a bad situation.

Similarly, Nicholas Piramal entered a joint venture (49:51) with Allergan Inc. to earn business for manufacturing bulk drugs. It also negotiated with the UK-based Baker Norton to earn business in the form of contract manufacturing. And it seems that the growth in contract manufacturing has come from mainly the efforts of companies such as Divi, Sashun and Nicholas Piramal India, which have been willing to accept even 'subordinate relationships' in their collaborations to get business of contract manufacture. See Table 7.7 for a glimpse into the pattern of CRAM activities being undertaken by large domestic pharmaceutical firms since the time of the adoption of TRIPS Agreement in India.

Table 7.7

Pharmaceutical Companies in CRAMS Activities in India

Company in Contract Research (excluding clinical trials)	*Clinical Trials*
Nicholas Piramal	Clingene (Biocon)
Aurigene (Dr. Reddy's)	Jubilant Clinsys (Jubilant Organosys)
Syngene (Biocon)	WellQuest (Nicholas Piramal)
GVK Biosciences	Synchron
Jubilant Organosys	Vimta Labs
Divi's Laboratories	Lambada
Suven Life Sciences	Siro Clinpharm
Dr. Reddy's Laboratories	Reliance Life Sciences
Vimta Labs	Asian Clinical Trials (Suven Life Sciences)

Source: *Annual Report and IDMA news 2007* (International Disease Management Alliance), URL *http://www.idma-assn.org/*.

In this context, it needs to be kept in view that the pharmaceutical fine chemicals (PFC) industry is also experiencing a period of development driven by changes in the demands of its major pharmaceutical clients and the desire to depart from the low profit areas of basic fine chemical manufacture. PFC companies have responded to recent pressures through a series of high value acquisitions increasing their size, core capabilities, geographical reach and the ability to buffer the pitfalls associated with late pharmaceutical withdrawals. Expansion of companies' core competencies and their geographical reach, in addition to the acquisition of new technologies and facilities, appear to have been the objectives of a number of recent acquisitions.

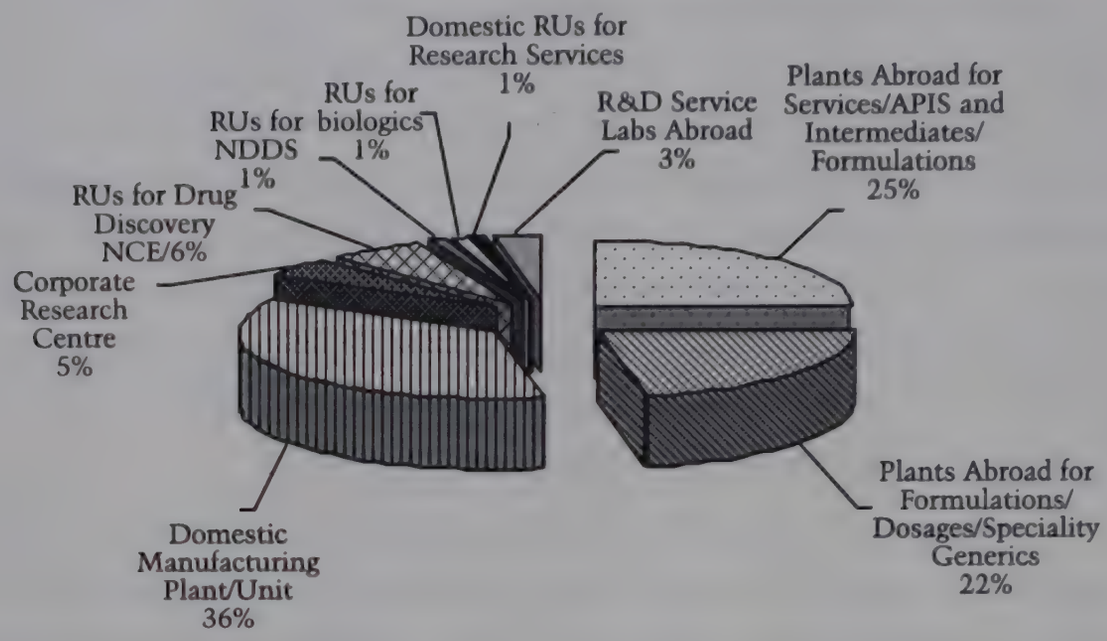
PFC companies are also thus involved in a longer-term process of restructuring that makes them to vacate the low profit areas of basic fine chemical manufacture for the benefit of Asian companies and to undertake a shift to the higher margin territories involving innovative technologies. Consequently, the big PFC producing firms have preferred to shift these low margin areas to Asia which, however, involves very little gain in respect of competence building for the Indian firms.

Capability Building through Foreign Facilities

Progress shown by these firms is in fact not very promising in acquiring capabilities for new drug development. In establishing research units abroad, these firms have done far less as compared to establishing manufacturing abroad. Those who have established their R&D facilities are far more for the purpose of dossier preparation for generic entry rather than for the development of new products. Further, they have been developing their plants abroad. This has again implications for the creation of coordination mechanisms and network alignment for the future development of learning and innovation trajectories. See Figure 7.1 for the emerging pattern of establishment of facilities for manufacturing and research abroad by these companies.

Figure 7.1

R&D and Manufacturing Facilities Established by Leading Indian Pharmaceutical Firms



Note: RUs: research units.

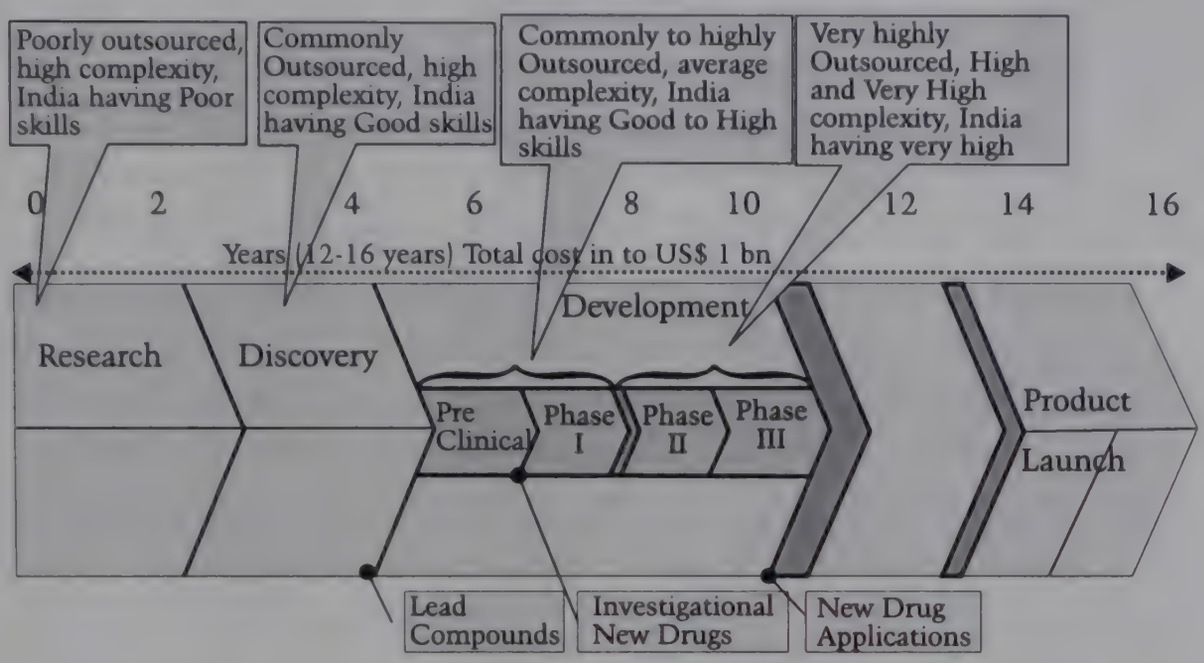
Drug Discovery and Development in Private Sector

While there are no two opinions that new product development is important, new product development research is an extremely high-risk proposition. India's domestic companies have just begun the journey in drug discovery. While the country has seen some success in selected companies, as expected the number of drug candidates that pass through subsequent phases is limited. The balance sheet size of Indian pharmaceutical firms is limited and currently Indian pharmaceutical companies cannot afford around US$ 1 billion required for drug development and clinical trial costs. The number of drug candidates that seem to have passed through post-licensing phases is even more limited. A clear strategy for developing skills in value chain of drug research is missing; domestic pharmaceutical firms do not have sufficient capabilities to move on their own in the global market. In the drug research value chain, there are key blocks like biology, chemistry, drug evaluation, pre-clinical trials and clinical trials. The system of drug discovery and development that the country needs would certainly have a role for the industry networks as well as the public sector system

of science. See Figure 7.3 for the changing system of drug discovery and development in India.

Figure 7.2

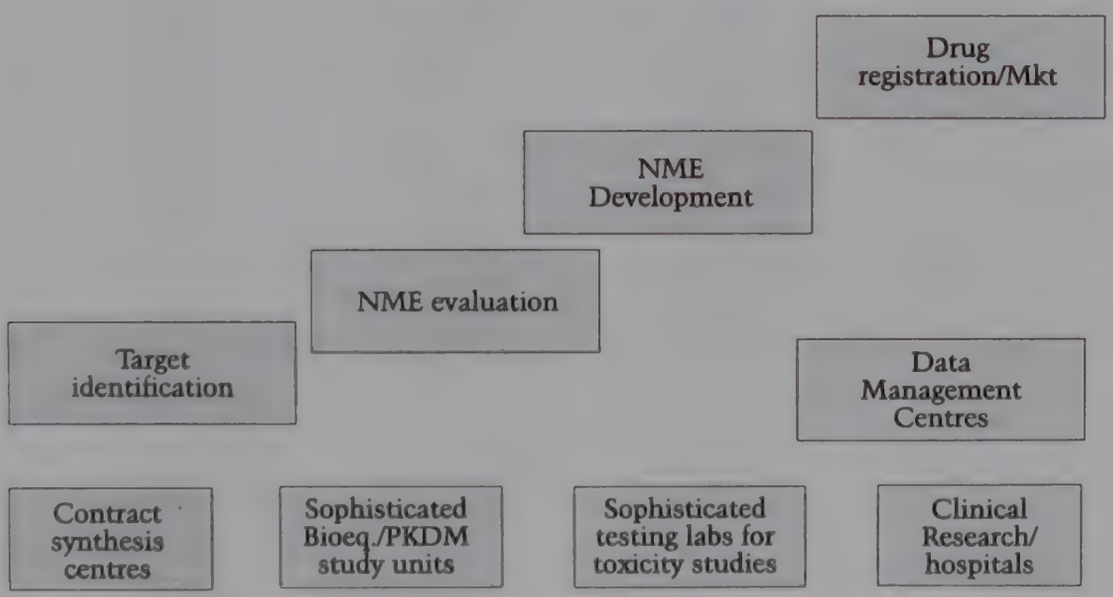
Drug Discovery Value Chain



Source: GoI (2008).

Figure 7.3

Key Areas in Drug Discovery



Source: GoI (2008).

The story of Indian new drug discovery in the private sector began in 1994 with Dr K. Anji Reddy of Dr Reddy's Laboratories (DRL), who was earlier a technocrat in the leading public sector firm namely Indian Drugs and Pharmaceuticals Limited (IDPL). DRL was responsible for setting up the first new private sector

drug lab at Hyderabad as a distinct facility. Table 7.8 provides the phase-wise status of compounds under development in the case of active domestic and foreign pharmaceutical firms in India during the period 1999-2009.

Table 7.8

Pattern of Phase-wise Clinical R&D Activities in the Case of Domestic and Foreign Pharmaceutical Firms Active in India, 1999-2009

Companies	*1999-2001*			*2002-2004*			*2005-2007*			*2008-09*			
	Compound Status/Phases												
	I	*II*	*III*	*I*	*II*	*III*	*I*	*II*	*III*	*I*	*II*	*III*	*Total*
Foreign (8 companies)	1	2	1		1	1	2	4	2	10	23	69	116
Domestic (15 companies)	1			9	3	1	19	17	12	27	21	47	157
Grand Total (23 companies)	2	2	1	9	4	2	21	21	14	37	44	116	273

Note: Compound Status/Phases: I, II, III.

Source: Data collected from each company's website and latest annual report of individual pharmaceutical companies and CTRI Clinical trial registry India.

Emerging evidence indicates that investment in product development activity is unevenly developing in respect of national science and technology (S&T) infrastructure of hospitals and medical colleges. Foreign firms are far more able to use the S&T infrastructure developed during the period of last 60 years. Further, it is also a matter of concern that the clinical R&D activity is concentrated in phase III stage where the gains with regard to competence development are extremely limited. An estimated 60 new compounds are also known to be in various phases of development and testing under the domestic Indian firms. Some of these compounds have been licensed in by the domestic companies from foreign firms. Needless to say, the activity of compound development and testing by domestic companies is quite small compared to world standards. Domestic pharmaceutical firms are just starting to pursue their phase I clinical trials in India. Much of the efforts of foreign pharmaceutical companies in clinical trials are in phase III. This means that the clinical research part of the national system of drug innovation is being far more valued for the patients that India can provide rather than for competencies that the system built on the basis of competencies of clinical research organisations (CROs), medical practitioners, colleges and hospitals

is usually known to be accomplishing in the case of cutting-edge drug innovation.

Further, it is also emerging that neither the domestic firms nor the above outlined system can really claim to have developed during the post-TRIPS period enough resources to pursue the cutting-edge drug innovation and take a new compound through all stages up to marketing. India is still weak in respect of the research capability required for the stage of drug discovery work; large domestic companies have only been pursuing those areas of drug discovery and development in a bigger way that lowers their costs and risk factors. This can be illustrated through the case of one of the DRL compounds. DRL is still one of the most determined domestic companies working on the national scene in the area of drug discovery and development. Strategy pursued is to find a new drug within an existing family that has been discovered—finding a compound that is analogous to a compound already discovered by Sankhyo from within the family of Giltazones. This strategy cuts down on the risk. A company can reduce some of the uncertainties of new drug research, though this may not produce a drug as big as a blockbuster.

The second strategy is out-licensing where the Indian company takes certain leads to pre-clinical stage. Then it may strike a deal with MNC that will have the right to market the compound in a particular market if all tests are cleared. The Indian company gets milestone payments for each stage of clinical trials, if the compound clears. All the big companies namely, Ranbaxy, DRL and Glenmark have followed the out-licensing route to develop new drugs. DRL has tried a deal with Novartis for further work on an anti-diabetic compound DRF 4158. Ranbaxy entered into a deal with Bayer for Cipro NDDS and RBx 2258 (BPH). Glenmark has tried a deal with Forest of North America and Tejin of Japan for compounds that could provide treatment for asthma. But the level of success obtained by these companies through the routes currently under perusal has not yet yielded the desired results in respect of new product development.

Contribution of the ties under development with the foreign companies is marginal to the actual development of firm-specific technological capability for new product development. Tables 7.9-7.11 indicate that adequate resources could not be leveraged from

Table 7.9

Status of Alliances, Collaborations and Acquisitions of R&D and Marketing by Indian Pharmaceutical Companies, 1999-2011

Company	Clinical and discovery R&D		Research Services	Marketing		Manufacturing Services
	Alliances/ Collaborations	Acquisitions		Alliances/ Collaborations	Acquisitions	
Cipla Ltd.	9		1	6	1	
Ranbaxy Laboratories*	14	2	3	37	15	1
Dr. Reddy's Laboratories	5	1	3	17	8	1
Lupin Ltd.	4			16	6	1
Biocon Ltd.	16			14	3	
Orchid Chemicals & Pharmaceuticals*	5	1	1	11	1	1
Cadila Health care	6	2		1	3	
Nicholas Piramal*	11	5	8	11	14	6
Glenmark Pharmaceuticals	4		1	4	10	
Matrix Laboratories*	2	1		6	6	
Ipca Laboratories	3			6	2	
Strides Arcolab		3		4	7	4
Sun Pharmaceutical		9	2	4	9	8
Wockhardt Ltd.				11	6	
Aurobindo Pharma		1		1	3	2

Note: * Companies are now become foreign companies after the acquisition of Ranbaxy by Daiichi Sankyo in 2009, acquisition of Matrix by Mylan in 2007, acquisition of Shantha Biotecnics by Sanofi Aventis in 2009, acquisition of Nicholas Piramal (Health Unit) by Abbott Laboratories, and acquisition of a part of Orchid Pharma by Hospira Inc., US.

Source: Data collected from news, press releases, websites and latest annual reports of individual pharmaceutical companies and Google News archive search. Data accessed as on April 2010.

the acquisitions and strategic alliances entered into by these firms for the upgrading of processes of drug discovery and development. Evaluation shows that even after the elapse of almost two decades, the learning and innovation making activities of these companies are successfully occurring only in respect of the development of non-infringing processes and low end incremental innovations which are required for the successful entry of domestic firms into regulated generic pharmaceutical markets of the US and Europe.

Table 7.10

Status of Alliances, Collaborations and Acquisitions in Competence Building/ Innovation Making by Indian Pharmaceutical Companies, 1999-2011

Company	*R&D*								*Total*
	Alliances/Collaborations				*Acquisitions*				
	RI/Academia		*Firm*		*RI/Academia*		*Firm*		
	DO	*FO*	*DO*	*FO*	*DO*	*FO*	*DO*	*FO*	
Cipla Ltd.	2		1	6					9
Ranbaxy Laboratories*	3	2		9				2	16
Dr. Reddy's Laboratories		1		4				1	6
Lupin Ltd.	1		1	2					4
Biocon Ltd.		2	1	13					16
Orchid Chemicals & Pharmaceuticals*				5				1	6
Cadila Health care		2		4				2	8
Nicholas Piramal*	4	2		5				5	16
Glenmark Pharmaceuticals				4					4
Matrix Laboratories*	1			1				1	3
Ipca Laboratories	3								3
Strides Arcolab								3	3
Sun Pharmaceutical							2	7	9
Wockhardt Ltd. Aurobindo Pharma								1	1

*Note:** Companies are now become foreign companies after the acquisition of Ranbaxy by Daiichi Sankyo in 2009, acquisition of Matrix by Mylan in 2007, acquisition of Shantha Biotecnics by Sanofi Aventis in 2009, acquisition of Nicholas Piramal (Health Unit) by Abbott Laboratories, acquisition of facilities for injectibles manufacturing and RD from Orchid Pharma by Hospira Inc., US.

RI: research institutes; DO: domestic companies; FO: foreign organisations.

Source: Data collected from, news, press releases, websites and latest annual reports of individual pharmaceutical companies and Google News archive search. Data accessed as on April 2010.

An assessment of the motives and outcomes of their international acquisitions, strategic alliances, collaborations and agreements confirms that the gains of these companies continue to relate far more to marketing and production of generics rather than R&D for product innovation. The emerging Indian pharmaceutical multinationals have not been able to acquire the firm-specific technological assets needed for the successful conduct of R&D activities for drug discovery and development from their interactions and linkages with foreign firms.

Table 7.11

Status of Alliances for the Provision of Research Services, 1999-2011

Company	*Research Services*				*Total*
	RI/ACA		*IND*		
	DO	*FO*	*DO*	*FO*	
Cipla		1			1
Ranbaxy Laboratories*	1			2	3
Dr. Reddy's Laboratories		1		2	3
Orchid Chemicals & Pharmaceuticals*				1	1
Nicholas Piramal	2			6	8
Glenmark Pharmaceuticals				1	1
Sun Pharmaceutical				2	2
Grand Total	3	2		14	19

Note: RI: research institutes; ACA: academics; IND: industry; DO: domestic companies; FO: foreign organisations.

Source: Data collected from, news, press releases, websites and latest annual reports of individual pharmaceutical companies and Google News archive search. Data accessed as on April 2010.

India does not seem to figure much in the increased strategic R&D alliance activity of the global biopharmaceutical and biotechnology firms. Saberwal (2009) showed in her survey of alliance activity that only eight companies were involved from India: Gland Pharma, GVK Bio, Odyessey (US entity), Advinus Therapetuics, Bharat Biotech, Serum Institute, Stride and Shantha Biotech. An explanation for this trend is due to the fact that in biopharmaceutical research, the distribution of capabilities is the major determinant of the partner and the mode of alliance.

Table 7.12

Disease Type-wise Product R&D Activities of Foreign Firms Active in India, 1999-2009

	1999-2001			2002-2004			2005-2007			2008-09			
	Disease Type												
	I	II	III	I	II	III	I	II	III	I	II	III	Total
Foreign companies (8 companies)	5			2			8	1		98	1	3	118

Note: Disease types: Type I—diabetes, cancer, metabolic diseases, hepatitis, influenza, cardiovascular, infectious diseases, inflammatory diseases, allergy, respiratory diseases.

"According to the World Health Organisation, diseases can be divided into three types. Type I diseases 'are incident in both rich and poor countries, with large numbers of vulnerable populations in each'. Type II diseases 'are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries'. Type III disease 'are those that are overwhelmingly or exclusively incident in developing countries'."

Source: Data collected from individual websites and latest annual reports of individual pharmaceutical companies and CTRI (Clinical Trial Registry India).

Further, at present under the route of wholly-owned subsidiary, Astra-Zeneca is the only example of drug discovery operations for tuberculosis (TB), a Type II disease. Of course, here too one needs to keep this in mind that these operations were started when Astra was an independent company. In fact, the Indian government induced Astra to start its operations as a joint venture with the government to work on TB-related drug discovery and diagnostic work. After its merger with Zeneca, the Indian operations are now taking place under the direct control of Astra-Zeneca. This is still an isolated case; foreign firms are unlikely to establish integrated drug discovery facilities for the diseases that affect disproportionately India (see Figure 7.12).

Therefore, the policy concern is whether drug MNCs should be allowed to use India merely as a cheap source of S&T manpower and patients and as a 'listening post.' Foreign pharmaceutical firms are unlikely to develop India as a location for the development of system integration capacity. Since in the new drug discovery paradigm, the system integration capacity is going to finally count[2]

2. Nightingale (2000) emphasises this by suggesting that the learning of system integration skills is a pre-condition of further competition in the development of innovative drugs in the global pharmaceutical industry today.

and if the development of this capacity cannot be expected to take place automatically, it is obvious that the foreign subsidiary mode in which the MNCs are now restructuring their investments should not be encouraged by the Indian government. The current expectations of global pharmaceutical firms are clear. Global pharmaceutical firms will prefer to selectively invest in the selected R&D operations namely bioinformatics and clinical research where by relocation it is possible for them to cut down the R&D costs without increasing information spillovers.

Available evidence from India suggests that in many cases, the MNCs appear to have preferred the route of R&D outsourcing from fully dedicated companies to reduce costs in respect of clinical trials and bioinformatics related R&D work. Presently only for the healthcare management and pharmaceutical services, the choice of MNCs has been to establish fully owned R&D subsidiaries. Establishment of operations for the implementation of clinical trials, data management and biostatistics by Quintiles, a leading pharmaceutical service provider, is an example.

Dr. Reddy's Group was the first domestic company to file the first two product patent applications for anti-cancer and anti-diabetes substances in the US. But even the DRL is not able to engage autonomously in drug development. It has been selling its rights to the partners abroad merely for the reason that it does not have the capacity to invest further. It has had to live with partners stopping midway the work on drug development and claiming that no further work is necessary. Examples of Wockhardt joining hands with Rhein Biotech GmbH, Germany, Ranbaxy shaking hands with Eli Lilly for development work, and Cipla undertaking custom synthesis, collaborations with Japanese and Swiss firms indicate the limitations of and opportunities available to Indian firms. At the moment, there are at least 10-12 Indian pharmaceutical companies that are working on the development of new products. An estimated 60 new compounds are known to be in various phases of development and testing. But not too many of these compounds are expected to be successful and are being abandoned and discontinued or further R&D work. In spite of 16 years of investment in research, no new drug has made it out of Indian domestic pharmaceutical

firms. See Table 7.13 for the changing status of NCE-based drug discovery pipeline of pharmaceutical firms active in India.

Table 7.13

Current Status of NCE-based Drug Discovery Pipeline

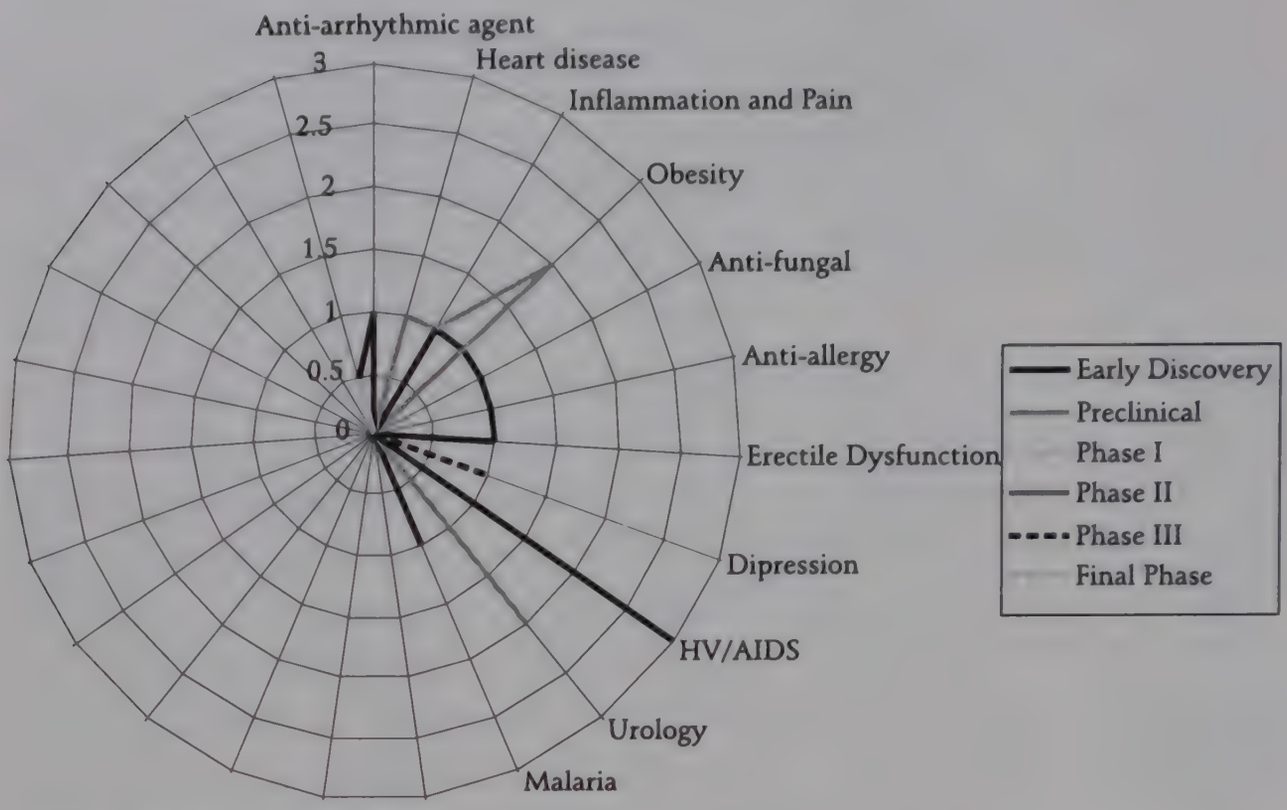
	Compound continuing				*Compound abandoned*				
	Pre-clinical	*Phase I*	*Phase II*	*Phase III*	*Pre-clinical*	*Phase I*	*Phase II*	*Phase III*	
Cardiovascular		1			1	1			3
Metabolic diseases/ diabetes	1	1	1	1	3	4	1		12
Cancer		1	2		4	1			8
Inflammatory diseases	1	1			1				3
COPD	1	1							2
Pain		2					1		3
Bone diseases		1	1						2
Tuberculosis			1						1
Malaria		1							1
Bacterial infection	2		1			1			4
Psoriasis			2	1					3
Dermatology			1						1
Urinary incontinence						1			1
Allergy/ asthma	1						1		2
Total	6	9	9	2	9	8	3		46

Source: Compiled on the basis of reported information in "Death of a dream", cover story in *Business World*, January 30, 2010, URL: *http://www.businessworld.in/bw/*.

Figure 7.4 provides details of the latest status of disease and phase-wise outcomes of new drug development activity of the Indian pharmaceutical firms. Much of the work is at an early stage of development; a large number of R&D activities correspond to pre-clinical stage of development. We can also see in the creation of R&D capabilities for new drug discovery and development within the Indian firms that they have a global market favouring R&D orientation.

Figure 7.4

Status of Disease- and Phase-wise Outcomes of New Drug Development Activity



Source: Same as Table 7.12.

Further, only a handful of firms have been able to increase their R&D investments in a significant way. R&D expenditure of the top 15 Indian pharmaceutical firms is nowhere near the expenditure being incurred by the generic companies of Israel and Europe. The top ranked domestic company Ranbaxy is now no more a domestic company. It has been sold by its Indian promoters to Daichi Sankhyo, a Japanese multinational. Further, even the other leading companies namely Dabur, Nicholas Piramal, Wockhardt and Shanta Biotech have also divested important parts of their pharmaceutical business to foreign companies. In many cases, these divestures have also involved R&D-based segments. The latest news is that Cipla is also negotiating the sale of its assets with foreign firms. While it is true that DRL, Glenmark, Lupin, Cadila, Wockhardt, Sun Pharma and Torrent are still around as integrated Indian pharmaceutical companies which have also built substantial foreign sales, an analysis of the current status of their new drug development clearly indicates that most molecules have not progressed very far. Many of them have been completely abandoned by the firms. Analysis undertaken of the disease focus and the status of progress confirms that the

Indian companies consider the domestic market to be of small size and not sufficiently attractive for taking up the development of new products in the drugs and pharmaceutical sector.

In recent years, ambitious new start up discovery firms backed by private equity investors such as Pune-based Novolead and Indus Biotech have also come up. They could succeed where Indian pharma's Goliaths wandered into and faltered (*Business World*, January 30, 2010). While these discussions about where the hopes lie in respect of new drug development have led some to suggest that India's first innovative drug could come instead from a new generation of pharmaceutical companies, is this the end or the beginning of the story? Whether the dream can be revived for the Indian domestic pharmaceutical firms is in need of rigorous analysis if the policy design is to be worked out appropriately.

Misalignment of R&D Activity of Private and Public Sectors with the Emerging and Future Needs of Indian Disease Pattern

Policy makers have also failed in tackling the challenge of realigning the R&D activity with the needs and gaps in R&D being experienced at home. While the community of public health specialists, clinicians and pharmacologists have been indicating in their respective studies the problems that need to be solved in respect of different types of disease burden by the public and private sector R&D units, R&D activities being undertaken in the public and private sector do not match very well with these priorities. This systemic gap is largely a result of the failures that have arisen at the level of the sector being unable to evolve jointly with all the relevant functions of innovation system in a systematic way. Mismatches continue to aggravate due to current focus being on the objective of profit making.

Analysis shows that therapeutic efficacy improvement, safer and less toxic drugs are not getting sufficient attention in respect of neglected diseases. This problem has also its roots located in the structure of domestic demand. There is also the problem of the norms of project selection within the system of public sector science system being formed on the basis of the markets that have been constituted for scientific reputation in the countries like the US and Europe.

As their research priorities are quite different, there are obviously mismatches arising with the needs at home. See the evidence provided in Table 7.14 on the influence of the structure of domestic demand on the pattern of process technologies that the CSIR laboratories contributed in the pre-TRIPS period for the manufacture of compounds needed to mainly serve the domestic market.

Table 7.14

Process Technologies Developed and Licensed to Industry by the Council of Scientific and Industrial Research

Type of Disease	*1965-1980*	*1981-1994*	*1995-2005*	*Total*
Type I	39	21	7	67
Type II	5	2	3	10
Type III	6	4	2	12
Others (not targeted at any type of disease)	1	1	3	5
Grand Total	51	28	15	94

Source: Abrol (2009).

Table 7.15

Disease Focus of New-Chemical-Entity-Based Drug Discovery Pipeline, 2009

Company	*Cancer*	*Metabolic Disorders*	*Brain/ Nervous System*	*Bone Diseases*	*CVS*	*TB*	*Malaria*	*Skin*	*Multiple Infections*	*Total*
Lupin Ltd.		1	1	1		1		2		6
Dr. Reddy's Laboratories	3	5		1	2				1	12
Wockhardt Ltd.								1	5	6
Glenmark Pharmaceuticals		2			1				1	4
Torrent Pharmaceuticals		1			1					2
Orchid Pharmaceuticals		1								1
Zydus Cadila		6								6
Piramal Health Care	1								1	2
Alembic Ltd.			3						1	4
Biocon Ltd.	1	1								2
Sun Pharmaceutical Industries									1	1
Ranbaxy Laboratories							2		6	8
GSK Pharmaceuticals	1		1						1	3
Total	6	17	5	2	4	1	2	3	17	57

Note: CVS: Cardiovascular.
Source: Company annual reports and websites, accessed on December 2009.

Today as the situation stands in India, the in-house industrial pharmaceutical R&D is largely directed to the needs of the western markets and much less to undertaking Type III R&D meant for neglected diseases of the poor in developing countries (see Figure 7.15). This is clear from the overwhelming nature of evidence available at glance in Tables 7.16-7.18. But there is more to the evidence available on the orientation of ties under development in Tables 7.9-7.11. These tables also show that all the important developments that we see in respect of the creation of R&D capabilities for drug discovery and development within the Indian firms have far more global market favouring R&D orientation. But it would not be wrong to point out in the case of domestic firms that their inventive activity is still better distributed in favour of domestic burden disease as compared to foreign firms.

Table 7.16

Disease-wise Product-Specific R&D Activities of Domestic Indian Firms, 1999-2009

	1999-2001			*2002-2004*			*2005-2007*			*2008-09*			
	Disease Type												
	I	*II*	*III*	*I*	*II*	*III*	*I*	*II*	*III*	*I*	*II*	*III*	*Total*
Orchid Pharmaceuticals Ltd.				2			6			2			10
Sun Pharmaceutical Industries Ltd.							2			7			9
Biocon Ltd.				2			4			6			12
Glenmark Pharmaceuticals Ltd.				1			5		1	7			14
Bharat Biotech Ltd.								1	1	3		2	7
Alembic Ltd.													-
Dr. Reddy's Laboratories Ltd.				7			2	1		15			25
Lupin Ltd.	1				1		4	4		4		1	15
Cadila Health care Ltd.							3	1		9			13
Piramal Health care Ltd.							7			5			12
Wockhardt Ltd.							1			2			3
Ipca Laboratories Ltd.										2	2		4
Aurobindo Pharmaceutical Ltd.													-

contd...

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	I	II	III	I	II	III	I	II	III	I	II	III	Total
Torrent Pharmaceuticals										1			1
Ajanta Pharma										7			7
Natco Pharma										2			2
Granules India Ltd.										1			1
SMS Pharmaceutical										10			10
Shanta Biotech							3		2	10	1		16
Panacea Biotech												2	2
Matrix Laboratories										3			3
Grand Total	1			12	1		37	7	4	96	3	5	166

Note: Disease type: Type-I, Type-II, Type-III.

Type I: diabetes, cancer, metabolic diseases, hepatitis, influenza, cardiovascular, infectious diseases, inflammatory diseases, allergy, respiratory diseases.

Type II: HIV/AIDS, tuberculosis, malaria.

Type III: leishmaniasis, trypanosomiasis, lymphatic filariasis, leprosy, diarrhoea (neglected diseases of the poor in developing world).

Source: Data collected from individual websites and latest annual reports of individual pharmaceutical companies and CTRI.

Table 7.17

Clinical Phases of Compounds for Various Diseases by Foreign and Domestic Pharmaceutical Industry during 2007-2009

Company	*Disease Type*			*Status of Trial/Phases*			
	Type I	*Type II*	*Type III*	*Phase I*	*Phase II*	*Phase III*	*Phase IV*
Domestic firms (16 companies)	65	3	2	5	20	35	9
Foreign firms (9 companies)	110	3	3	12	23	12	9

Note: Disease type: Type-I, Type-II, Type-III.

Type I: diabetes, cancer, metabolic diseases, hepatitis, influenza, cardiovascular, infectious diseases, inflammatory diseases, allergy, respiratory diseases.

Type II: HIV/AIDS, tuberculosis, malaria.

Type III: leishmaniasis, trypanosomiasis, lymphatic filariasis, leprosy, diarrhoea.

Status of involvement of domestic and foreign firms in the trials (Phase-I, Phase-II, Phase-III, Phase-IV).

Source: Clinical Trial Registry Analysis (CTRI) 2007-2009.URL: *http://ctri.nic.in/Clinicaltrials/index.jsp*.

Table 7.18

Pharmaceutical Projects, Patents and the Pattern of Matches with National Burden of Disease, 1992-2007

Major Therapeutic Area/Disease/Health Condition	*Share in the Total Burden of Disease (%)*	*Domestic Pharmaceutical Project (%)*	*Foreign Pharmaceutical Project (%)*	*Disease-wise Individual Domestic Patents out of Total Domestic Patents (in % for Pharma Companies)*	*Disease-wise Individual Domestic Patents out of Total Patents (in % for Pharma Companies)*	*Disease-wise Individual Foreign Patents out of Total Foreign Patents (in % for Pharma Companies)*	*Disease-wise Individual Foreign Patents out of Total Patents (in % for Pharma Companies)*
1	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Diabetes/metabolic disease	0.7	24.51	17.26	12.73	12.67	20	0.084
Cancer	3.4	10.05	8.81	5.6	5.57		
Tuberculosis	2.8	1.18		0.50	0.50		
Malaria	1.6	2.36		0.93	0.92		
HIV/AIDS	2.1	0.59	0.23	0.84	0.84		
Inflammatory diseases/ infectious diseases/injuries	16.2	11.83	5.21	44.56	44.36		
Respiratory diseases	1.5	4.73	5.61	1.1	1.09		
Bone disease	-	4.73	6.63	1.27	1.26		
Brain disorders	8.5		0.56	10.18	10.14	40	0.16
Ulcer	-			0.5	0.50		

contd...

...contd...

1	2	3	4	5	6	7	8
Psoriasis	-			0.33	0.33		
Cardiovascular	10	0.59	10.12	8.05	8.18	20	0.084
Maternal and prenatal problems/ childhood disease	16.0	1.34		0.25	0.25		
Diarrhoea	8.2	1.77		0.08	0.084		
Depression	-			3.56	3.55		
Allergy	-			1.78	1.77		
Hepatitis	-		1.81	0.16	0.16		
Leprosy	0.1						
Blindness	1.4						
Oral diseases	0.5						
Prosthetic hyperplasia	-			1.01	1.014		
Others	25.4	30.17	18.18	6.45	6.42		

Source: USPTO from 1992-2007, Company websites and data available on the burden of disease from GOI. *http://www.uspto.gov/.*

At the moment, the dynamics of biotechnology in India seems to be dependent on the overall movement of internationalisation of R&D. Contract research is becoming one of the route through which the domestic pharmaceutical companies are trying to build their competence in drug discovery and clinical research. Outsourcing markets in clinical trials are growing rapidly. The contract research scene is also livening up in drug discovery. Because of many short-term benefits, it is obviously quite tempting to direct the industry mainly for these markets in countries like India. The examples of DRL and Biocon are especially useful for discussion on the conditions for gains to accrue from the contract work being undertaken by these two companies. Both these companies have created several entities, each of them corresponding to a different strategy. DRL is involved in the development of recombinant DNA-based products and has an internal programme of biotechnology-based drug targets discovery. It has also set up a company named Molecular Connections, and a contract research company named Aurigene, involved in chemical and biological research for drug discovery. Similarly, Bicon too, whose core activity is the manufacturing of industrial enzymes, has set up a contract research subsidiary named Syngene, and a clinical research organisation named Clinigene.

However, as far as the contribution of these domestic firms to meeting the product development challenge for neglected diseases is concerned, analysis is clear that the current level of opportunities which limit Aurigene, GVKbio and Syngene to cloning the genes and getting the genes to express would not allow these companies to build an industry capable of doing cutting-edge biotechnology research. At the moment, their mother companies do not have any intention of interfering with their subsidiaries because of the agreements of confidentiality signed by them with the partners who have outsourced the part of drug discovery or clinical research to them. This means that no technological information can circulate between the company in charge of contract research work and the parent company involved in its own research.

Emerging Orientation of Public-Private Partnerships (PPPs) of Indian firms

Public-private partnerships (PPPs) is the latest new buzzword in the system of health research and technology development. In India, the New Millennium Indian Technology Leadership Initiative (NMITLI) of Council of Scientific and Industrial Research (CSIR), Drugs and Pharmaceuticals Research Programme (DPRP) and Technology Development Board (TDB) of Department of Science and Technology (DST) and Small Business Innovation Research Initiative (SBIRI) of Department of Biotechnology (DBT) constitute the main examples of PPPs. Strong experience has been gathered through these schemes in respect of the determinants of success in implementation of PPPs.

A large number of NMITLI-based PPPs have preferred to catalyse health innovations only as a vehicle for the domestic industry to attain mainly global leadership position in selected niche area by synergising the best competencies of publicly funded R&D institutions, academia and private industry. In the last six years, NMITLI has supported 42 R&D in various fields including new targets, drug delivery systems, bioenhancer and therapeutics for psoriasis, tuberculosis, pain management in osteoarthritis, insulin sensitisation in diabetes mellitus Type II and process of Tamiflu, etc., with about 287 partners, 222 in public sector and 65 in private sector with an estimated outlay of over ₹ 300 crore.

Analysis of SIBRI efforts (37 cases till May 2008) shows that there is not much focus for diseases of Indian interest though a couple of cases pertain to malaria and typhoid. Similarly, in the case of DPRP, it is also known that the government had to add a special grant-in-aid programme for the promotion of research on neglected diseases because in the earlier years, the programme was unable to attract domestic companies to work on these areas.

Conceived in 2003, the Golden Triangle partnership is also now receiving special budgetary support for an integrated technology mission focused on the development of Ayurveda and traditional medical knowledge that synthesise modern medicine, traditional medicine and modern science. In this way, efforts on traditional

medicine have also picked up momentum. The CSIR and ICMR are working with the Department of Ayurveda, Siddha, and Homeopathy to bring out safe, efficacious, and standardised classical products for identified disease conditions. New Ayurvedic and herbal products for diseases of national/global importance are also being pursued. Innovative technologies are being used to develop single and poly-herbal-mineral products, which have the potential for IP protection and commercial exploitation by national/multinational pharmaceutical companies. Areas identified are limited to mainly *rasayana* (rejuvenators/immunomodulators) for healthy aging, joint disorders, memory disorders, bronchial allergy, fertility/infertility, cardiac disorders (cardio-protective and anti-iatherosclerotic), sleep disorders, and diabetes.

Current Direction of Neglected Disease R&D

Recently, India has also witnessed a spurt of research investments for neglected diseases. But much of this increase in R&D investment for neglected diseases has occurred on account of external push. The following are some of the international partners:

- WHO Special Program for Research and Training in Tropical Diseases (TDR)
- Global Alliance for Tuberculosis Drug Development (TB Alliance);
- Medicines for Malaria Venture (MMV) for Malaria vaccine;
- International AIDS Vaccine Initiative (IAVI) for HIV/AIDS Vaccine;
- Institute for One World Health (IOWH)
- Drugs for Neglected Diseases Initiative (DNDi) for sleeping sickness, Chagas disease, leishmaniasis, and malaria;
- Program for Applied Technology for Health (PATH) for JE vaccine;
- Concept Foundation for microbicides.

The MMV is collaborating with Ranbaxy for developing anti-malarials. The IOWH is collaborating with the ICMR in the clinical trials of paromomycin for visceral leishmaniasis.

Earlier in 2003-04, in the segment of neglected Type III diseases, India had also taken another important initiative for development of new generation vaccines for cholera, malaria, tuberculosis, Japanese encephalitis (JE) and HIV/AIDS. Projects initiated as a part of Jai Vigyan programme of the Ministry of Science & Technology are known to be following a different route of PPPs where the collaboration in technology development involves the element of collaboration with partners located in the advanced world for technology transfer. Under this initiative, the government had also signed a number of technology licensing agreements to obtain the technologies required for tackling the diseases of the poor.

Of the 21 technology missions for integrated R&D that would benefit rural people, the development of new generation vaccines is an important time-bound initiative. The main objective is to develop candidate vaccines for cholera, rabies, Japanese encephalitis, and tuberculosis, malaria and HIV infections using novel strategies. These include recombinant proteins; DNA vaccines; recombinant/peptide vaccines for cholera, malaria, tuberculosis, JE, and rabies (for animals and humans); and preventive/therapeutic DNA candidate vaccine(s) for HIV infection.

Impact of the Current Pathways on the Use of the Government R&D Schemes

While the industry is known to be complaining of government funding for the direct benefit of R&D in industry being rather small, it can be however seen that they are not even utilising the existing schemes in a big way. Medium burden diseases are a major focus of the projects submitted by the industry. This is because of the attraction of these diseases on account of markets being more attractive due to the worldwide emphasis on many of those diseases at the level of R&D funding. See Table 7.19 for the pattern of diseases covered by these firms while using the government-funded

programmes and schemes initiated for the benefit of pharmaceutical innovation.

Table 7.19

Pattern of Firm-level R&D Projects from Government-Funded Programmes and Schemes

Funding Agency Programme/Scheme	*High Burden*	*Medium Burden*	*Low Burden*	*Total*
DPRP	23	30	13	66
BIPP	6	5	1	12
SBIRI	2	14	10	26
Grand Total	31	49	24	104

Note: DPRP : Drugs and Pharmaceuticals Research Programme;
BIPP : Biotechnology Industry Partnership Programme;
SBIRI : Small Business Innovation Research Initiative.

Source: DPRP, BIPP, SBIRI websites, data accessed in November 2011.

Table 7.20 indicates that most of the emerging Indian pharmaceutical multinationals have not been leveraging the government funding for undertaking industrial R&D. More than half of these firms chose to ignore the schemes formulated by the government industrial research financing altogether. There were only six firms out of 14 firms that took projects funded by the government for the development of facilities and activities required to be undertaken for the development of new drugs. But even they accounted for just 15 projects in the portfolio of 104 projects sanctioned by the government. It is clear that these firms have not come forward to use the government schemes for R&D and innovation of therapeutics for tackling the priority diseases.

Lack of interest in the schemes from the emerging Indian pharmaceutical multinationals is the case even when the government has agreed to cede to the collaborating firms the ownership of intellectual property rights (IPRs). Some of these firms have now been sold by its promoters to foreign firms. It is obvious that the national links of these firms are only getting weakened rather than being strengthened. Certainly the outward foreign direct investment (OFDI) connections of the strategies of the emerging Indian pharmaceutical multinationals are affecting

adversely the plans that the policy makers have for the development of the national system of innovation for the benefit of Indian pharmaceutical industry.

Table 7.20

Firm-wise Pattern of Government Funding by Burden of Diseases, 2005-2011

	DPRP			*BIPP*			*SBIRI*		
	High Burden	*Medium Burden*	*Low Burden*	*High Burden*	*Medium Burden*	*Low Burden*	*High Burden*	*Medium Burden*	*Low Burden*
Total number of projects in different classes of disease burden	23	30	13	6	5	1	2	14	10
Torrent Pharma	-	1	4	-	1	-	-	-	-
Ranbaxy Laboratories	-	5	-	-	-	-	-	-	-
Strides Arcolab	1	-	-	-	-	-	-	-	-
Lupin Pharma	1	-	1	-	-	-	-	-	-
Cadila Health care	-	3	-	-	-	-	-	-	1
Biocon Ltd.	-	-	-	-	1	-	-	-	-
Total	2	6	5	-	2	-	-	-	1

Note: DPRP : Drugs and Pharmaceuticals Research Programme;
BIPP : Biotechnology Industry Partnership Programme;
SBIRI : Small Business Innovation Research Initiative.

Source: DPRP, BIPP and SBIRI websites, data accessed in November 2011.

Identifying the strengths and weaknesses of existing modern medical products, the strategy seeks to develop new products to address gaps; formulate an appropriate R&D strategy for standardisation, quality control, IP, and other related issues; take up toxicity/efficacy studies in government laboratories, medical colleges and universities; prepare detailed dossiers of effective formulations; and negotiate with an identified industry partner to begin commercialisation after clinical trials are carried out using standard protocols. This ambitious multiagency programme proposes to spend more than ₹ 350 million in the next three years. Several areas have already been identified and research is underway.

Concluding Remarks

Contrary to expectations of the policy makers, the growing global integration is failing to generate the 'best case conditions' predicted for the Indian pharmaceutical sector. Analysis of the evidence in the post-TRIPS technological behaviour of Indian pharmaceutical industry clearly confirms the apprehensions of not-for-strong IPR favouring interest groups. Strong IPRs have not favoured India with the claimed benefits of increased access to good quality FDI, technology transfer, overseas product R&D and stimulation of domestic investment in R&D for product innovation for local needs.

Evidence also shows domestic and foreign pharmaceutical companies do not have any big plan to invest in R&D on their own on the development of medicines related to local needs of India. Their incorporation into the emerging international division of labour is leading the domestic pharmaceutical production and the linked innovation systems to move only further away from the goal of development of medicines for developing countries health conditions. Therefore, policy makers will have to seek significant changes on the side of supply of innovation capacities if their new strategies for industrial up gradation are to obtain significant success. Policy makers need to get the private sector to coordinate with the public sector in the creation of a programme for upgrading of the innovation capacities to play a positive role in the drug development for the diseases of the poor in India. Policy makers will have to target the direct support for R&D and facilities for clinical trials. Domestic firms should not get incentivised for inappropriate product targets.

Dependent relationships being forged through excessive reliance on low quality contract work in both manufacturing and research would have to be discouraged. It would not be possible for them to grow beyond a point through the routes of generics and contract work in research and manufacturing. These routes can be used to supplement the strategy of expanding the domestic market, but to mainly depend on these routes for further growth would take the domestic firms away from the real needs-based innovation. There

also would not be much increase in the domestic private sector's R&D expenditure. In the face of more opportunities for short-term gains, very few firms would have the incentive to compete with their international partners. It is likely that most domestic firms would ultimately settle down to accept the role of junior partners in the new game of proteomics and genomics based innovation wherein the R&D platform/tools are already monopolised *via* the route of strong IPRs.

Prospects for domestic R&D for neglected diseases and conditions would improve only under the conditions where the constraint of market size has been suitably eased for the benefit of local pharmaceutical firms. To alleviate the constraint of small market size, the Indian government must step in to improve the demand conditions. In the recent period, the health expenditure has been declining across the board in India. This is a direct consequence of the implementation of neo-liberal fiscal strategy. It is too much to expect the domestic pharmaceutical firms whose revenues are insecure to contribute to R&D investment for neglected diseases under the situation of declining public health expenditure.

The channels of interaction for learning, competence building and innovation making are therefore still mainly subject to the push and pull for innovation efforts arising out of the strategies of domestic and foreign pharmaceutical firms. The use of strategy of strong IPRs is one of the most important institutional changes that the Indian policy makers can expect to come in the way of knowledge diffusion. Their adverse effect on the size of market for local firms has to be suitably alleviated. Markets for knowledge and technology are by no means neutral space; policy interventions for industrial upgrading have to take into account that there is an international division of labour being constituted through the route of outsourcing. Innovation systems must stay clear of the traps that this division of labour is laying down for domestic firms. Policy makers have failed to undertake an industry-wide view, to assess second order capabilities and to evaluate the complementarities and linkages developing within the national system of innovation.

To take a more definite view on the policy alternatives that are now under consideration, a critical evaluation is needed of the contribution of policy design to the developments taking place with regard to the sale of domestic firms by foreign buyers. Policy makers need to reassess the potential of global integration in a systemic manner. The implications of continuing with a public policy designed to accelerate the pathways of growth chosen for the globalisation of domestic pharmaceutical industry during the post-TRIPS Agreement period are also required to be characterised in a systemic way which means the assessment should include an evaluation of the problems of capacity and system building and realignment of innovation priorities.

Finally, policy makers would have to try getting the domestic firms to concentrate their efforts on the real needs-based innovations and those strategies that would largely free the Indian firms from getting into dependent relationships with the foreign firms. With the intervention of public sector agencies, the situation can change and head for better. It is possible to conceive a route of PPP to give a momentum to the field of discovery and development research in the area of pharmaceuticals that would take care of the priorities of national public health and neglected diseases of the poor of developing world as a whole.

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8

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Access to Essential Vaccines in India

Introduction

Vaccines are critical in a health system to prevent newborn and child-related deaths, disabilities and diseases. India's national immunisation programme that began in 1978, called the Expanded Programme of Immunisation (EPI), included six vaccines against diphtheria, pertussis, tetanus, poliomyelitis, typhoid and childhood tuberculosis. In 1985, the EPI was renamed the Universal Immunisation Programme (UIP). Under the new UIP, measles was included and typhoid was excluded.

Beginning from 2006, one dose of Japanese encephalitis vaccine has been incorporated into the UIP for children aged 1-15 years in high-burden districts. Similarly, three doses of hepatitis B vaccines are also administered to children in 10 states and three union territories. Pentavalent, a combination of vaccines against five diseases (diphtheria, pertusis, tetanus, hepatitis B and haemophilus influenza B), has been introduced in the southern states of Tamil Nadu and Kerala; recently this has been extended to six other states.

The UIP is now geared to meeting the growing demand arising from over 26 million births being added every year. An estimated ₹410 crore was spent on the UIP in 2011-12. Traditionally, paediatric vaccines have been the mainstay of health systems across nations, although in recent years, adult vaccines are emerging as one of the major medical interventions. Ironically, while India is the lead producer of vaccines in the world, it is also home to the maximum

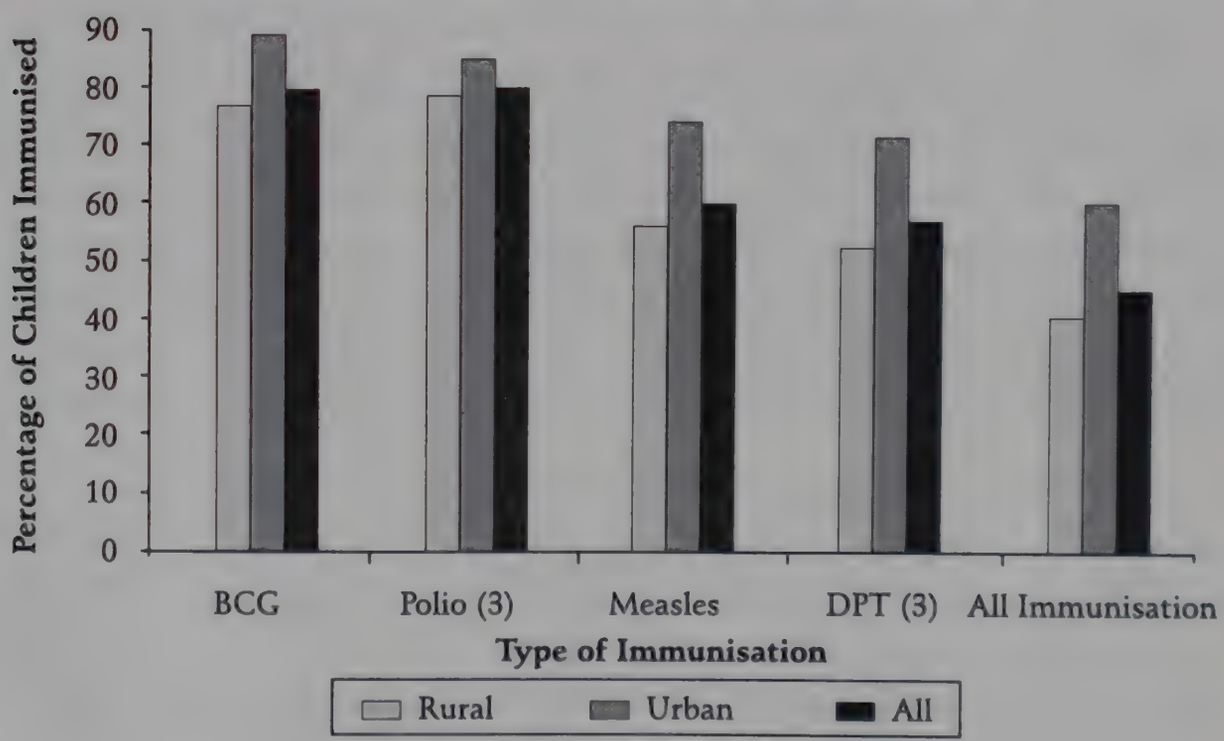
number of child deaths, partly owing to lack of immunisation coverage.

Current Trends and Inequalities in Immunisation

India is likely to miss the Millennium Development Goal (MDG) target on child mortality by a substantial margin partly due to lack of immunisation coverage. The percentage of children covered with all vaccines stood at 43.5 per cent in 2005-06, a marginal improvement from 35.4 per cent in 1992-93. The polio coverage is by far the best, improving dramatically from 54 per cent in 1992-93 to over 78 per cent in 2005-06. This is followed by the BCG (Bacillrs Calmette-Guerin) tuberculosis vaccine, whose coverage increased substantially from 62 per cent to 78 per cent for the same period. Measles coverage went up steadily from 42 per cent to 59 per cent for the same years. The DPT (combination vaccine against diphtheria, pertussis and tetanus) coverage of all three rounds, however, is the most disappointing, with almost stagnant growth from 52 per cent in 1992-93 to 55 per cent in 2005-06.

Figure 8.1

Immunisation Coverage in India by Region, 2005-06



Note: Children immunised in the age group of 12-23 months.

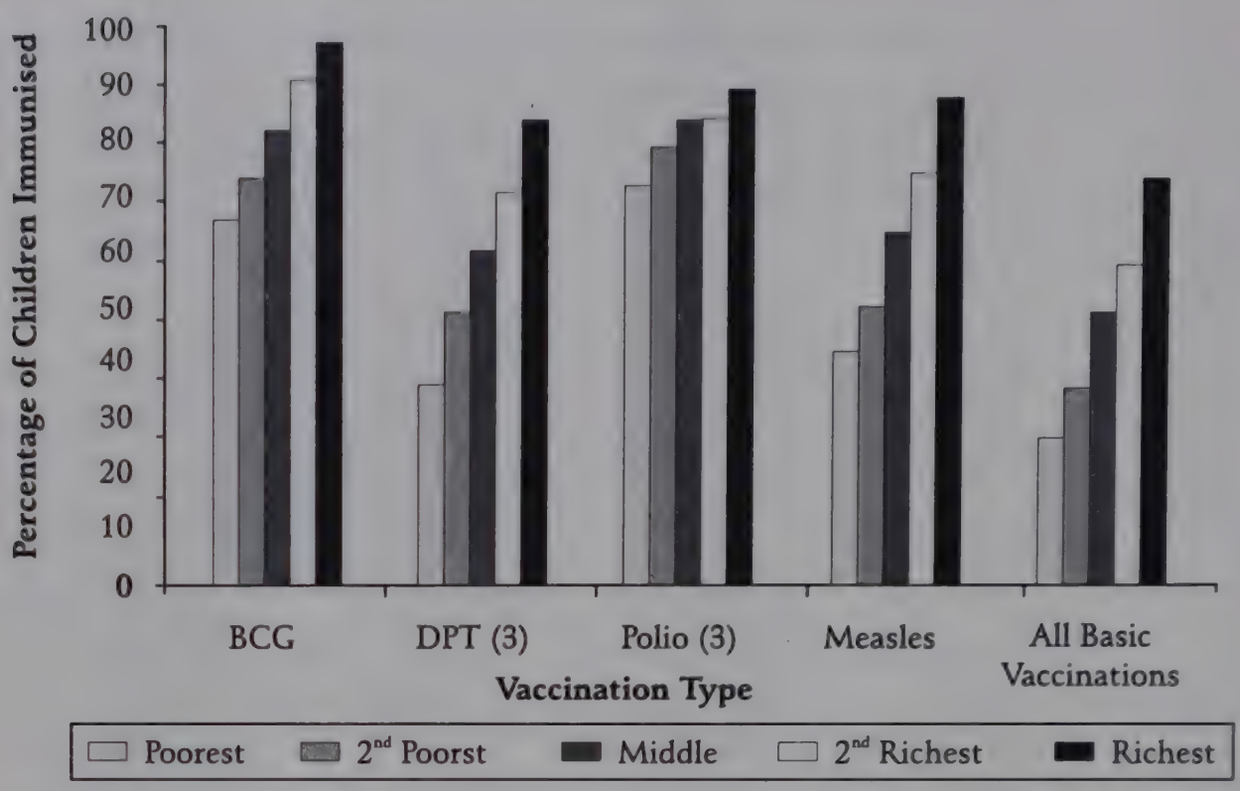
Source: *Third National Family Health Survey* (NFHS-3), 2005-06.

The immunisation coverage is marked by substantial inequalities between genders, regions and socioeconomic groups. Although only about 44 per cent of children aged 12-23 months were fully immunised in 2005-06, less than 40 per cent of all children were immunised in rural areas as against the urban coverage rate of 58 per cent (Figure 8.1). The gender bias continues to exist in immunisation coverage rates as well, with 41.5 per cent of girls immunised as against 45.3 per cent of boys in 2005-06. State-wise coverage reflects uneven improvement in immunisation rates, with Uttar Pradesh recording half of the national average. In fact, Nagaland is the only state that lags slightly behind Uttar Pradesh at 21.0 per cent. The star performer is Tamil Nadu, with the best rate of 81.0 per cent, closely followed by Kerala and Himachal Pradesh at 75.3 per cent and 74.2 per cent respectively. One of the major limitations in low-performing states such as Uttar Pradesh, Bihar, Rajasthan, Orissa and Jharkhand is that the last point of the cold chain stops at the block level, which covers a population of about 200,000, while in other states the cold chain reaches the primary-health-centre level, which caters to a population of 30,000.

In terms of socioeconomic characteristics, data from the Third National Family Health Survey (NFHS-3) clearly demonstrate the power of education. Children with mothers who had 12 or more years of completed education (75.2%) are thrice as likely to receive vaccines as those with mothers who did not have any education (26.1%). Children born in the Muslim community (36.3%) are half as likely to be vaccinated as their Sikh counterparts (67.3%). Scheduled tribes (STs) children, due to socioeconomic and geographical disadvantages, are covered only to the extent of 31 per cent as against the other forward caste groups that recorded higher coverage rates of almost 54 per cent. In terms of quintile groups, evidence from the NFHS-3 demonstrates that the richest groups, due to affordability and proximity to public/private health facilities, are thrice as likely to receive vaccines for their children as against the poorest of the population with roughly 26.1 per cent coverage rates (Figure 8.2).

Figure 8.2

Quintile-wise Immunisation Coverage Rates in India, 2005-06



Note: Children immunised in the age group of 12-23 months.

Source: NFHS-3, 2005-06.

Barriers to Access to Essential Vaccines in India

Several barriers to access to essential vaccines are identified in the Indian scenario. The key impediments are the following:

- inadequate financing of primary vaccines,
- unreliable and inefficient procurement and supply chain systems,
- rising prices of vaccines,
- production constraints,
- neglect of research and development, and
- shifting focus to non-UIP vaccines.

The rest of the chapter discusses some of these key barriers that are identified here with recent evidence while policy options are also outlined.

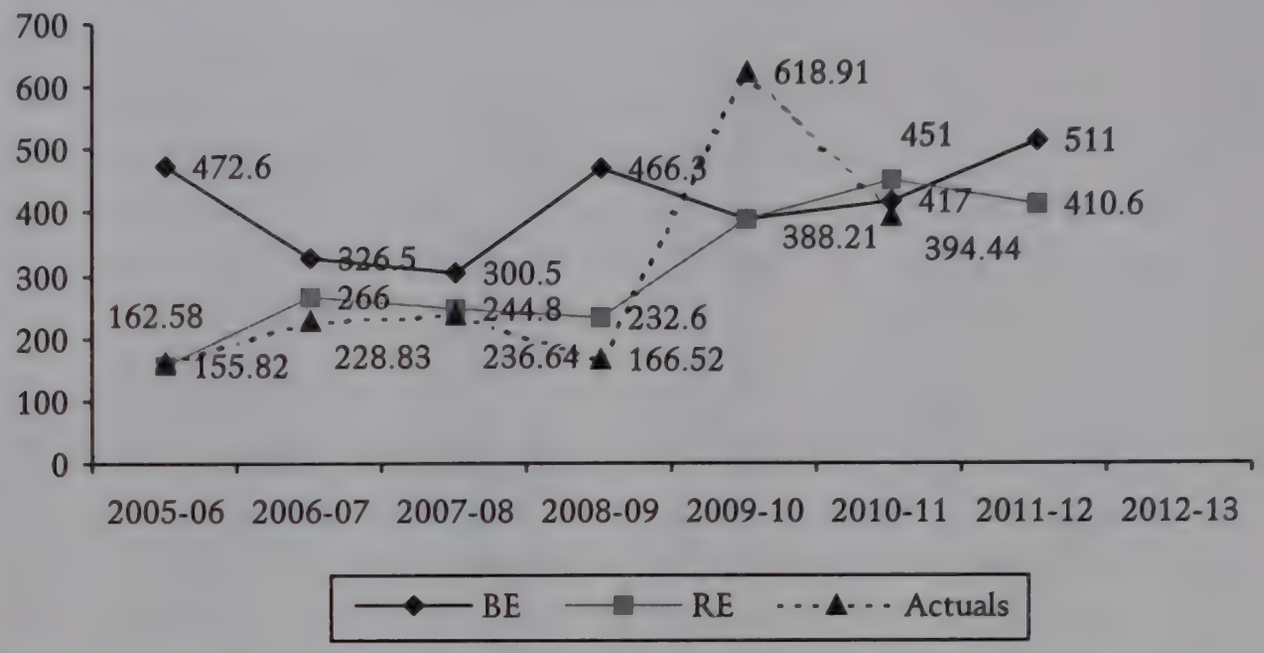
India has traditionally underinvested in public health, expenditure on which currently stands at 1.2 per cent of GDP. The amount of resources allocated to procure and distribute essential medicines, vaccines and supplies in the public health system is extremely inadequate, as only roughly 10 per cent of all government expenditure is on drug procurement. Since the bulk of vaccines are procured and distributed by the central government, with state governments having an insignificant role, the resources have been inadequate.

In 2005-06, the central government allocated approximately ₹ 162.58 crore for procuring vaccines against the budgeted figure of ₹ 472.6 crore, which works out to a little over one-third (Figure 8.3). In the following two years, the actual expenditures were only about 70 per cent of what was budgeted. Interestingly, in 2008-09 and 2009-10, the actual expenditure on vaccines fluctuated widely from 36 per cent to 159 per cent during the respective periods.

The actual expenditure on routine immunisation accelerated substantially from ₹ 162.58 crore in 2005-06 to nearly ₹ 619 crore in 2009-10, with a sharp drop in 2008-09. The sharp decline in expenditure in 2008-09 was due to the suspension of three public sector vaccine manufacturing units and the eventual drop in procurement of vaccines from them. In the following year, 2009-10, with the government having to procure vaccines from the private market to continue the immunisation programme, the cost of the programme substantially accelerated, leading to a phenomenal increase in the government expenditure. However, in 2010-11, as the public sector units resumed production of primary vaccines, the actual expenditure declined slightly below the budgeted and revised expenditure. In 2011-12, it is expected that the central government would spend to the tune of ₹ 410 crore.

Figure 8.3

Trends in Allocation of Central Government Expenditure on Immunisation



Source: (a) Budgeted expenditure (BE) and revised expenditure (RE) figures are from Government of India, Demand for Grants, Ministry of Health and Family Welfare, respective years.

(b) Figures for actual expenditure in 2009-10 and 2010-11 are from Demand for Grants Vol. II, for 2005-06 to 2008-09 from National Health Profile, Central Bureau of Health Ministry of Health and Family Affairs, New Delhi, Intelligence, *cbhidghs.nic.in*.

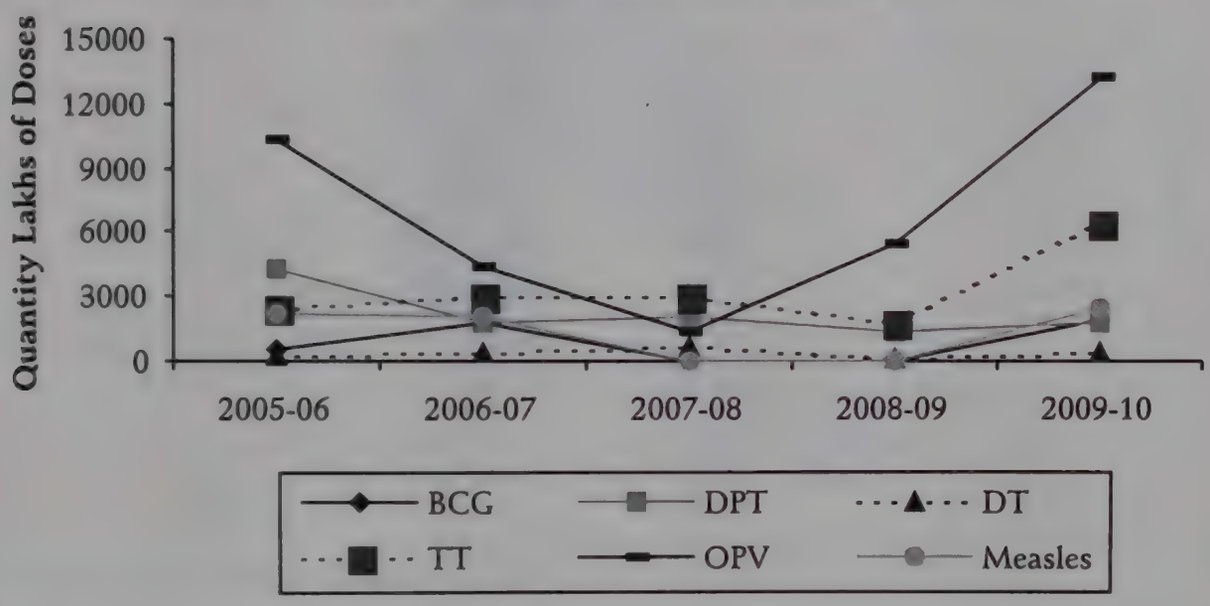
Current Trends and Pattern of Vaccine Production and Consumption

India has traditionally been the leading producer and supplier of primary vaccines [including vaccines for BCG, DPT, OPV (oral polio vaccine), DT (diphtheria and tetanus), measles and tetanus] not only for domestic use, but also a large quantity is also exported to several countries. Although only around half of the country's children are administered all primary vaccines, even if all Indian children were to be immunised, the domestic production would still be adequate with enough left over for export. While domestic private industry is a significant manufacturer and supplier of vaccines, the contribution of public sector manufacturing units in producing and meeting domestic demand and in continuously supplying as a pre-qualified manufacturer to international organisations including the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) is worth observing.

However, as Figure 8.4 reveals, production of vaccines suffered seriously in 2008 and 2009 owing to the shutdown of key public sector vaccine manufacturing units. The three vaccine-making institutes whose manufacturing licences were suspended in January 2008 were the Central Research Institute in Kasauli, the Pasteur Institute of India in Coonoor and the BCG Vaccine Laboratory in Guindy. The principal reason behind the closure of the public sector units was that it was reported that these units were not in compliance with good manufacturing practices (GMP) as per schedule M of the Drugs and Cosmetics Rules, 1945. The non-compliance is related to structural, process and documentation deficiencies. Although a new vaccine technology park is being commissioned in Chennai, the suspension of the three vaccine units has since been revoked and they have started operating again.

Figure 8.4

Trends in Primary Vaccine Production in India, 2005-2010



Source: Respective reports of National Health Profile, Central Bureau of Health Intelligence.

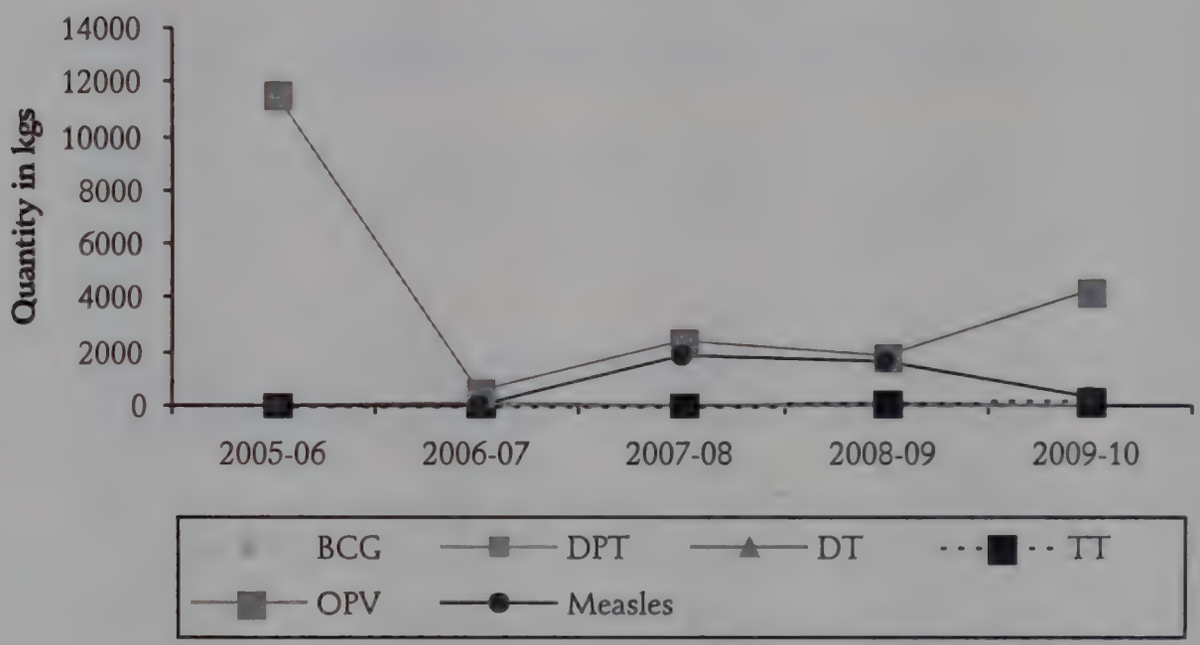
Due to the closure of the public sector units, the immunisation programme suffered a serious setback in 2008-09, as production and supply of primary vaccines was disrupted. Until the units stopped production, they had been the principal source of supply for the UIP. The BCG Vaccine Laboratory alone, for instance, was reported to be able to meet the BCG vaccine requirement for the country. These three units, two of which have been in existence for over a century, had never been the focus of attention with regard to the quality of products supplied by them. Past audits had never

found any discrepancies in the quality of vaccines, in terms of both efficacy and safety, until the recent closure.[1] Although these units have resumed production, it is a grim reminder of a misguided policy that needs to be avoided in the future.

In view of its self-sufficiency in manufacturing vaccines, India's vaccine imports were previously insubstantial. Figure 8.5 shows almost insignificant imports of primary vaccines prior to 2008-09 and even after. Imports of measles vaccines, which were substantial before 2005-06, witnessed a sharp decline in 2006-07 only to again increase in the following years. Similarly, polio vaccine (OPV) imports have been stepped up significantly due to the government's major drive to eliminate polio cases in the country.

Figure 8.5

Trends in Imports of Primary Vaccines by India, 2005-06 to 2009-10



Source: Directorate General of Commercial Intelligence, Ministry of Commerce and Industry, respective years.

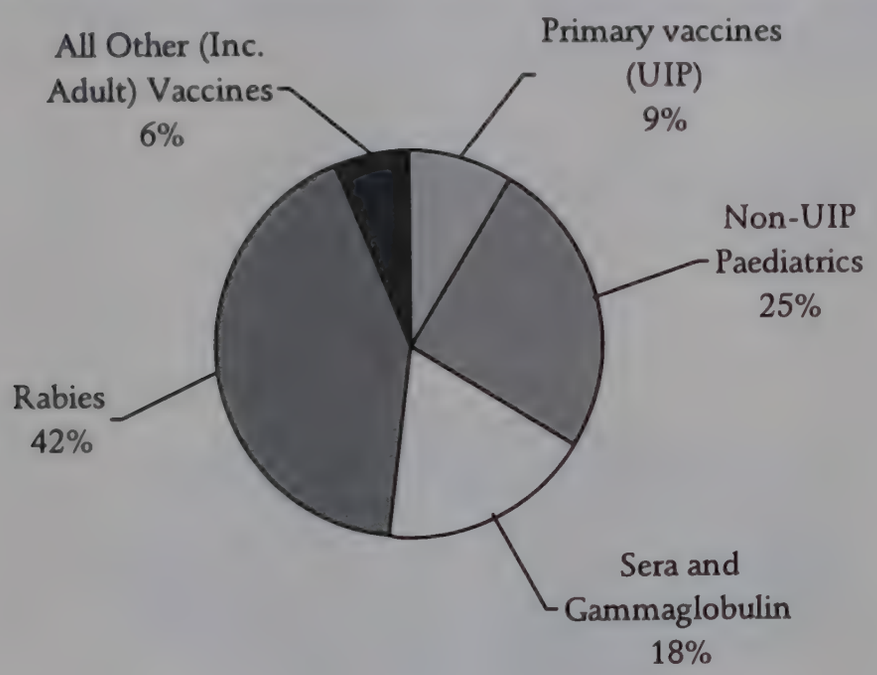
It is interesting to note that despite India's drug market being largely in the private domain, with private sector delivery much more preponderant and people therefore incurring substantial out-of-pocket expenditures, this has not been the case with vaccines, as the foregoing evidence points to a considerable government role in terms of financing, procuring and distributing them to cover

1. For a comprehensive view on the suspension and the functioning of the three public sector vaccine-producing units, refer to Madhavi (2008).

a large section of population. However, as Figure 8.6 reveals, the role of the private market is gradually beginning to appear on the scene. Although the private market's share is still less than 10 per cent of the total primary vaccine market, the non-UIP segments continue to thrive in the private open market. This is a cause for considerable concern, as the financial burden of households is set to rise substantially while inessential vaccines are being prescribed and used indiscriminately in the private sector. Evidence of the efficacy and even the disease burden with which some of the non-UIP vaccines are associated is still to be established.

Figure 8.6

Composition of Vaccines in the Private Market in India, 2008



Source: Estimated from IMS Health, 2008.

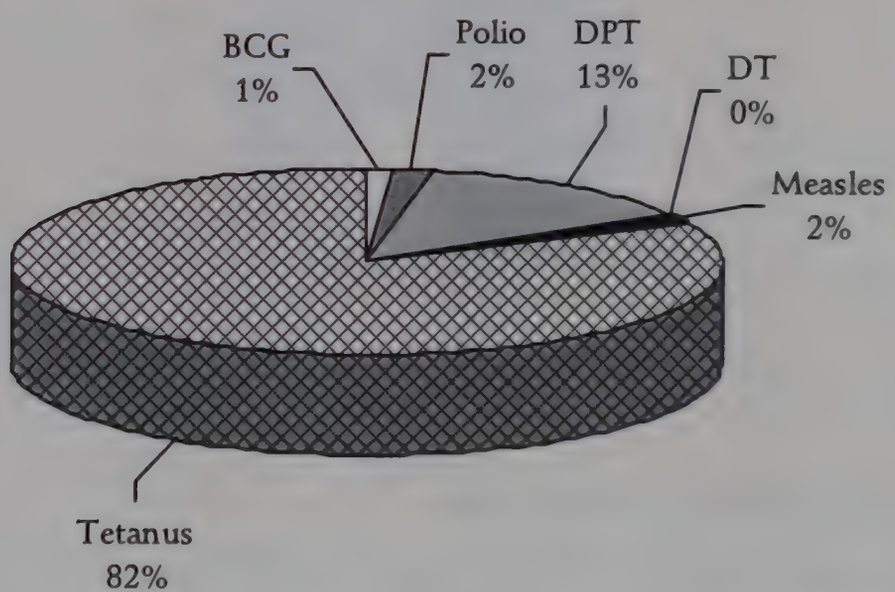
According to data from market researcher IMS Health, the private sector vaccine market was worth ₹ 275 crore in 2008. However, this does not include vaccines sold by the private stockists to institutions such as medium and large hospitals in the private sector. It is interesting to observe that during the same period, 2008-09, the government spent a similar amount, ₹ 258 crore, for procuring primary vaccines. The primary vaccine segment constituted only 9 per cent of the overall private market, while the dominant share of the private market is found in anti-rabies vaccine which alone constituted 42 per cent. Sera and gammaglobulin

accounted for 18 per cent of the private vaccine market. Some of the newer non-UIP paediatrics accounted for one-fourth of the overall private market. Adult vaccines have also begun to appear in the market, accounting for less than 6 per cent of the market.

The primary vaccines market in the private sector was worth approximately ₹ 25 crore in 2008. According to Figure 8.7, tetanus vaccine accounted for the largest share of 82 per cent, followed by DPT which accounted for 13 per cent. Measles and polio, on the other hand, accounted for nearly 2 per cent each in the entire primary vaccines segment sold in the private market, while the BCG segment accounted for 1 per cent. These trends point to the continuing dominant role being played by the government in procuring and administering primary vaccines towards the goal of immunising every child in the country.

Figure 8.7

The Share of Primary Vaccines in the Private Market



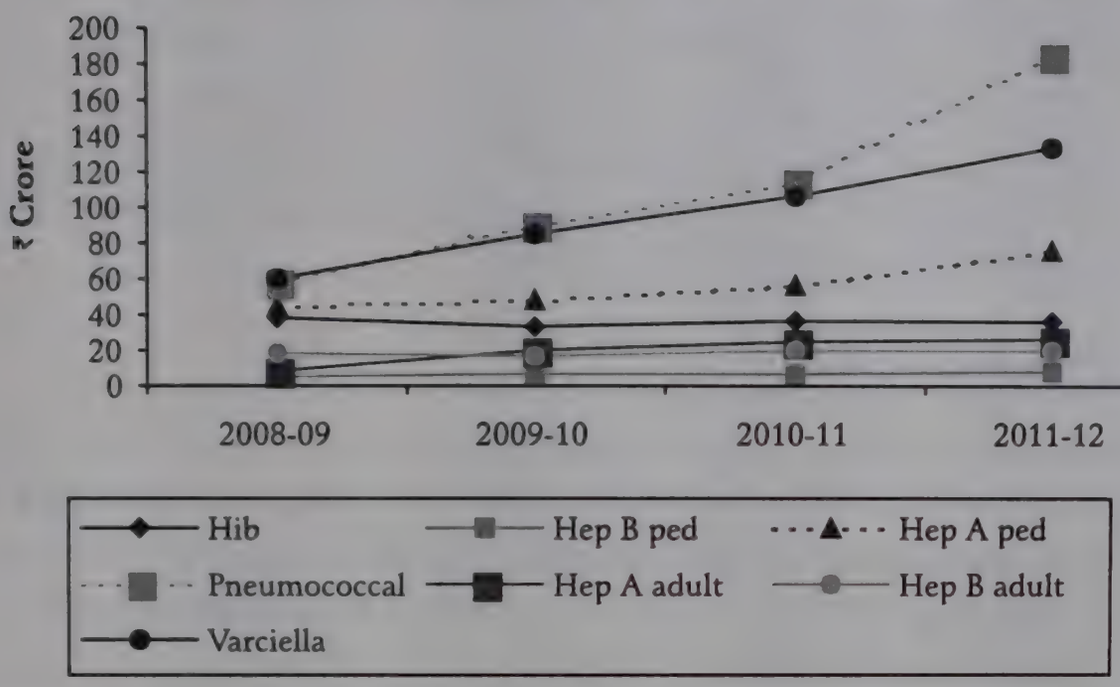
Source: Estimated from IMS Health, 2008

In recent years, the private sector market is increasingly seen to cater to the non-UIP segment of vaccines, which was worth ₹ 55 crore in 2008, more than double the primary vaccine market. The non-UIP market in the private sector is currently concentrated largely on hepatitis B vaccines, as adult vaccines appear to have captured a large segment of the private market. Hepatitis B, both adult and paediatrics, along with hepatitis A constitute the largest

market share. The Hib (haemophilus influenzae type B) vaccine is also gradually making its presence felt strongly, while the rising role of pneumococcal vaccine in the private market also needs to be noted (Figure 8.8).

Figure 8.8

Trends in Growth of Non-UIP Vaccines in the Private Market



Source: Estimated from IMS Health, 2008.

The debate about the inclusion of hepatitis B in the UIP in some states based on disease burden, cost-effectiveness, etc., is still continuing in the country.[2] The votaries of its inclusion into the UIP have been largely successful in pushing this vaccine through the private market, as the evidence underscores this trend above. Similarly, in recent years, the rotavirus vaccine is being pushed into the market and its inclusion into the UIP is being strongly promoted. Approximately half a million deaths due to rotavirus infection are reported: a significant share of which is found in the Indian population. However, recent studies in India do not provide sufficient evidence and the efficacy of new vaccines is questioned in the Indian population (Gladstone *et al.*, 2012).

Recent years have also witnessed a plethora of combination vaccines being promoted aggressively by the pharmaceutical

2. For a comprehensive debate and evidence on hepatitis B's inclusion in India and other countries, see Madhavi (2003).

companies. These cocktail vaccines are apparently sold at exorbitant prices in the private market. Pharmaceutical companies often combine UIP vaccines with non-UIP vaccines, which is expected to create artificial scarcity for UIP vaccines, and this tendency is likely to result in the backdoor entry of expensive non-UIP vaccines into the UIP scheme. According to Puliyel and Madhavi (2008). "The combination of DPT with hepatitis B raises the price of DPT immunisation 17 fold. Moreover, the relative safety and efficacy of these cocktail combinations are much lower than their individual counterparts. Yet, we have many cocktail vaccines flooding the market including DTP-IPV, DTP-HB, DTP-Hib, DTP-HB-Hib, DT-Hib, DTP-Hib-IPV, and DTPHB-Hib-IPV."

Summary and Conclusion

Despite being one of the leading producers of vaccines, India has high child mortality rates due partly to poor immunisation coverage. There is only 44 per cent coverage of all primary vaccines, and the coverage is marked by substantial inequalities between genders, regions and across socioeconomic groups. Inadequate financing of the UIP, inefficient procurement and unreliable supply chains are partly responsible for the poor coverage of the UIP in several states. With approximately 26 million children being added to the population every year, the annual ₹ 410 crore expenditure on the UIP is way below the expected spending.

India has been one of the major manufacturers of vaccines, especially the public sector units which supply primary vaccines not only for domestic needs but also for export. However, the recent policies and the closure of three vaccine-making public sector units in 2008 have put vaccine security under threat. Although the suspension of these units has since been revoked, not only were vaccine supplies disrupted, owing to dependence on private domestic players, but the prices of vaccines also increased substantially, which left a huge hole in the central government financing.

Even as the country is struggling to attain full immunisation coverage, efforts are being made to include unnecessary and

expensive non-UIP vaccines into the national immunisation programme. Without going into the specificities of disease burden, efficacy, safety and cost-effectiveness, several pharmaceutical industry lobbies are trying to make their way into the UIP by gaining back-door and front-door access to suit commercial interests.

The recent trend of combining one or two primary vaccines with non-UIP vaccines is attributed to efforts to gain control over the country's routine immunisation programme. Taking advantage of poor design and implementation and lack of resources for the national immunisation programme, which has been the mainstay of the government, the private vaccine market has been gaining gradual control over the years. However, the private healthcare system not only provides limited primary vaccines, but the private pharmaceutical industry has been aggressively pushing non-UIP and combination vaccines to the general public. The larger implication of these strategies is that necessity and efficacy aspects are not adequately taken into account, leading to a larger financial burden on households, which are already straddled with substantial out-of-pocket expenditures.

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9

SAKTHIVEL SELVARAJ

Pharmaceutical Regulation in India

Introduction

The drug regulatory structure in India spans several key activities of pharmaceutical control from providing licences to new products, regulating production and sale of licensed products for safety and efficacy, and regulating clinical trials of new molecules to regulation of banned, bannable and inessential drugs, regulating unethical promotion of medicines, price controls, product patent regulation, etc. The complex and intricate chain beginning from product innovation through production to sale and consumption of drugs calls for a coordinated and transparent regulatory response. Unfortunately, India's present drug regulation is characterised by weak structure, poor infrastructure, lack of skilled human resources, archaic legislation and multiple authorities, leading to poor implementation of rules and regulations. Currently, the Drugs and Cosmetics Act of 1940 and the Drugs and Cosmetics Rules of 1945, and the Drugs and Magic Remedies (Objectionable Advertisements) Act of 1954 which are amended from then on are the critical legislations that pertain to the functioning of the Drugs Controller General of India (DCGI) and the Central Drugs Standard Control Organisation (CDSCO). A recent report of the Parliamentary Standing Committee on the Functioning of the CDSCO pointed out several shortcomings and deficiencies. It marshals evidence of the 'systemic and manmade' shortcomings in the country's drug regulatory mechanism [Government of India (GoI), 2012].

Multiple agencies are involved in pharmaceutical regulation. Issuing new product licences is the prerogative of the CDSCO under the Ministry of Health and Family Welfare (MoHFW). The

same organisation, which is headed by the DCGI, is also responsible for regulating clinical trials in the medical colleges and hospitals. On the other hand, the power to regulate production and sale of medicines, especially with regard to ensuring safety and efficacy, is with the state drug controllers. A substantial regulatory structure is also vested under the Department of Pharmaceuticals (DoP) under the Ministry of Chemicals and Fertilisers. The DoP is expected to regulate not only drug prices through its National Pharmaceutical Pricing Authority (NPPA) but also unethical drug promotion, given that the department is expected to be the authority directly involved in promotion of the drug industry. Interestingly, the Ministry of Commerce and Industry is normally engaged in pharmaceutical trade negotiations and intellectual-property-related negotiations bilaterally and multilaterally.

Licensing and Regulation of Medicines

One of the key components of pharmaceutical regulation is registration/licensing of medicines. It is a process by which a national authority (MoHFW) approves the use of a medicine in India, after having considered the available evidence of the medicine's safety, quality and efficacy. It is thus primarily concerned with protecting public health. It has been highlighted that pre-marketing assessment of safety, quality and efficacy is however only one component of a medicines regulatory system. In addition, attention must be paid to ongoing assessment and inspection of the entire pharmaceutical supply chain (including manufacturers, importers, exporters, wholesalers, distributors and final sellers), maintenance of a register of approved products and post-marketing surveillance (including random quality checks and pharmacovigilance systems), control over the promotion and advertising of medicines, and the provision of medicines information.[1] In India, the DCGI under the MoHFW is responsible for licensing and standards (approval of new drugs, provision of standards, quality control over imported drugs, coordination of the activities of state drug control organisations, uniformity in enforcement of the Drugs and Cosmetics Act), whereas the regulation of manufacture, sale and distribution of

1. Srivastava (2008).

drugs is primarily the concern of the state governments. The respective roles and responsibilities of the central and state governments are elucidated in the Drugs and Cosmetics Act, 1940.

The central government's DCGI grants market authorisation to three categories of drugs: investigative new drug, new drug and follow-on products. However, for a biological drug, the Ministry of Environment and Forests reviews the environmental impact assessment of the production process to ensure that safety procedures are in place for the drug. For a drug that uses recombinant DNA technology, the Department of Biotechnology under the Ministry of Science and Technology is involved. The Department of Biotechnology approves pre-clinical studies and recommends human clinical trials to the DCGI. The DCGI grants permission for phase I,. II and III trials. For new drugs discovered in India, it is mandatory to conduct phase I-III clinical trials as required under Schedule Y of the Drugs and Cosmetics Rules, 1945, whereas for drugs discovered in other countries, it is a mandatory requirement to submit phase I data from the relevant country. Once the phase I data is submitted for review to the DCGI, the DCGI gives permission to repeat phase I and/or conduct phase II trials. A firm may use phase III data from another country but it is mandatory to still conduct phase III trials in India. For a follow-on or generic product, bioequivalence tests are required.

In a multi-country study of drug regulation, the World Health Organization (WHO) has observed that regulatory practice suffers from three types of common imbalance: (i) over-concentration on pre-market rather than post-market monitoring (e.g., of adverse reactions); (ii) too much focus on registration and inadequate emphasis on regulating the distribution system; and (iii) far more attention given to inspection of manufacturing practice rather than distribution channels.[2] This is true for the Indian regulatory system as well. In India, each state has its own drug control organisation that is responsible for drug quality and a system of licensure for the manufacture, sale and distribution of drugs within that state.[3]

2. WHO (2003).

3. Government of India (2003).

This has resulted in varying procedures and standards as imposed by state licensing authorities (SLAs), a situation which has seen some producers apply for licences from compliant SLAs if their own state is unwilling to grant a licence quickly or on reasonable terms, giving them an opportunity to obtain drug approval in one state from where it can be sold throughout the country. Also, there is a severe shortage of human resources for testing drugs and licensing producers, which has implications for the quality of medicines. Schedule M of the Drugs and Cosmetics Act lays down the Good Manufacturing Practices (GMP) guidelines to ensure consistent quality standards is maintained. However, its implementation has not been adequate as several of the small scale industries do not conform to GMP standards. Nevertheless, it has been reported that the Indian Drug Manufacturers' Association and several other drug production organisations (Small and Medium Pharmaceutical Industry Confederation, representing the small-scale drug industry) are critical of GMP certification because investing in GMP standards could be expensive. The current infrastructure is grossly inadequate to cope with the numbers of drugs, producers, pharmacies and prescribers.[4]

Counterfeit/Spurious Medicines

The weakness of the regulatory mechanism and institutions has led to a situation where the quality and safety of Indian medicines has been put at stake. Moreover, dissidents are cleverly mixing up issues like spurious drugs, counterfeit drugs or lookalike drugs, not-of-standard drugs and unaccounted inter-state movement of drugs to magnify the problem of 'spurious drugs.' By mixing up intellectual property issues (trademark violations), tax violations (inter-state movements) and technical issues (storage problems can make drugs substandard) and spurious drug manufacturing, the campaigners are seriously threatening the existence and credibility of the Indian small-scale drug manufacturing sector. The figures on counterfeit medicines quoted in the media range anywhere from 0.5 per cent to 30 per cent of overall drugs produced in the Indian market. However, these are totally unsubstantiated reports. As per

4. Ibid.

the government's own estimates,[5] substandard medicines ranged from 8 per cent to 10 per cent and the existence of spurious drugs from 0.2 per cent to 0.5 per cent during 1995-2003 (Government of India, 2003). In a recent national survey conducted by the CDSCO (2009), the extent of spurious drugs in retail pharmacy is shown to be far below the projections made by various media, WHO and other studies, i.e., only 0.046 per cent (11 samples out of 24,136 samples) (Table 9.1).

Table 9.1

Prevalence of Spurious and Substandard Drugs in India, 1995-96 to 2007-08

Year	*Tested*	*Substandard quality*	*Spurious*	*Percentage of substandard quality*	*Percentage of spurious drugs*
1995-96	32,770	3,490	100	10.64	0.30
1996-97	38,936	3,189	94	8.19	0.24
1997-98	32,936	2,979	157	9.04	0.47
1998-99	38,936	3,189	94	8.19	0.24
1999-2000	35,570	3,666	115	10.31	0.32
2000-01	36,947	3,088	112	8.36	0.30
2001-02	38,824	3,458	96	8.96	0.25
2002-03	36,314	3,395	125	9.34	0.34
2003-04	38,313	2,402	67	6.3	0.30
2004-05	49,287	3,695	144	7.5	0.29
2005-06	41,494	3,017	145	7.3	0.35
2006-07	42,354	2,718	66	6.4	0.16
2007-08 (upto Jan 2008)	38,313	2,402	67	6.3	0.17

Source: Central Drugs Standard Control Organisation CDSCO (2009).

5. Substandard medicines are pharmaceutical products that do not meet their quality standards and specifications. While a spurious drug is classified as under:
   a. if it is manufactured under a name which belongs to another drug; or
   b. if it is an imitation of, or is a substitute for, another drug or resembles another drug in a manner likely to deceive, or bears upon it or upon its label or container the name of another drug, unless it is plainly and conspicuously marked so as to reveal its true character and its lack of identity with such other drug; or
   c. if the label or container bears the name of an individual or company purporting to be the manufacture of the drug, which individual or company is fictitious or does not exist; or
   d. if it has been substituted wholly or in part by another drug or substance; or
   e. if it purports to be the product of a manufacturer of whom it is not truly a product.

Clinical Trials and Pharmacovigilance

The current concerns with respect to public health impacts of clinical trials are yet to be fully addressed. The regulatory mechanism which is expected to track the conduct of illegal and unethical clinical trials is far from adequate and perfect. The clinical trial registry, intended to bring about transparency in the conduct of clinical trials in the country, is also in its infancy. It has also been argued that the government should expedite the preparation of the bill that specifically looks at the protection of human volunteers in clinical trials and establish a central committee of experienced researchers for policy implementation, comprehensive policy guidelines for clinical trials, rules and regulations for toxicology studies, and a host of fiscal incentives.[6] In any case, clinical trials rarely involve a number of patients sufficient to make sure that less common side-effects and adverse drug reactions are picked up by the time a drug enters the market. This can only be addressed through post-marketing surveillance. India lacks a robust post-marketing surveillance or phase IV trial (pharmacovigilance system) which examines issues of safety and ongoing technical support of a drug after it receives licensing permission. Finally, the effectiveness of the National Pharmacovigilance Programme remains unknown (Patvardhan, 2005).

Inessential and Irrational Use of Medicines

Rational use of drugs requires that patients receive medications appropriate to their clinical need, in doses that meet their own individual requirements for an adequate period of time, and at the lowest cost to them and their community.[7]

Irrational use of medicines includes cases in which: (i) a medicine is prescribed where none was needed, (ii) medicines are not prescribed according to Standard Treatment Guidelines, or ineffective or unsafe medicines are prescribed, (iii) effective and available medicines are underused, (iv) medicines are used incorrectly, etc. The irrational use of medicines has an adverse

6. Parliament Committee Report (2013).

7. WHO Conference of Experts, Nairobi. WHO (1985).

impact on the outcome of therapy and cost and may therefore cause adverse reactions or negative psychosocial impacts.

The broad issue of irrational medicine[8] use also includes production, sale and consumption of banned/unsafe and bannable medicines. The likelihood of adverse reactions outweighs the therapeutic effects when unsafe medicines are prescribed. Examples include the use of anabolic steroids for growth and appetite stimulation in children or athletes, while in many countries, dipyrone (metamizole) or analgin, a drug banned in most developed countries, is used indiscriminately in both health facilities and the community for several minor ailments. Moreover, some internationally banned medicines are still being marketed in India (Table 9.2).

Table 9.2

Banned Drugs available Freely in the Market

Drug	*Indications*	*Reason for Ban*
Analgin	Analgesic	Can cause bone marrow depression
Cisapride	Acidity, GERD, constipation	Can cause irregular heartbeats
Furazolidone	Anti-diarrhoeal	Carcinogenic
Nimesulide	Painkiller, fever	Hepatotoxic
Piperazine	Anthelmintic	Can cause nerve damage
Phenylpropanolamine	Cough and cold	High doses can lead to stroke
Nitroflorozone	Antibacterial cream	Carcinogenic

Source: Parliament of India (2013).

And then there are medicines with doubtful efficacy or ineffective medicines. These are medicines with little or no therapeutic value and no clinically proven evidence is available about their use. Examples include excessive and unnecessary use of multivitamin preparations or tonics, use of appetite stimulants (cyproheptadine and buclizine HCl) in children, and use of digestants (given to boost digestion) which contain concentrations

8. Kindly also refer to chapter 6.

of amylase, papain, pepsin or pancreatin that are generally not suitable in an acidic medium. Overdosage of appetite stimulants may produce hallucinations, central nervous system (CNS) depression, convulsions and even death.

Fixed Dose Combinations

In addition to banned and ineffective drugs, the market is flooded with various irrational fixed dose combinations (FDCs). An FDC is defined by WHO as "a combination of two or more active ingredients in a fixed ratio of doses. This term is used generically to mean a particular combination of APIs [active pharmaceutical ingredients] irrespective of the formulation or brand. It may be administered as single entity products given concurrently or as finished pharmaceutical products."

Advantages of FDCs include:

(i) Combination medicines have the advantages of combination therapy as well as advantages related to reducing the number of pills to be consumed in a day.

(ii) Reduced administration costs stemming from simplified packaging, fewer prescriptions, and lesser dispensing time and cost.

(iii) Reducing the number of pills diminishes the complexity of the regimen, so that improved patient adherence is expected with FDCs.

(iv) FDCs can improve compliance in the treatment of chronic infectious diseases, where partial adherence can lead to the development of drug-resistant strains, treatment failure and a threat to public health. An example of this is the treatment of tuberculosis and HIV/AIDS.

(v) The side effects of one medicine can be reduced by combining it with another medicine in an FDC (e.g., carbidopa reduces the side effects of levodopa).

(vi) The efficacy of one medicine can be synergistically increased by combining it with another (e.g., the combination of estrogen and progesterone in oral contraceptives; the

combination of sulfamethoxazole and trimethoprim; pyrimethamine and sulfadoxine for the treatment and prophylaxis of falciparum malaria).

However, often the most widely prescribed FDCs are reported to not only have a rational basis but are mostly analgesics, multivitamin combinations, and cold and cough mixtures. Some examples of irrational FDCs available in today's market are combinations of anti-bacterials and anti-amoebics, multivitamin preparations, painkillers often combined with caffeine, tonics containing incorrect proportions of vitamins and minerals, FDCs of nimesulide with other drugs, cough suppressants and expectorants in the same cough mixtures, etc.

Licensing of Fixed Dose Combinations

As per the Drugs and Cosmetics Act and Rules, the CDSCO is responsible for granting approval for 'new drugs.' FDCs which are new in India are also considered to be "new drugs" as per Rule 122E of the Drugs and Cosmetics Rules as included in 1999. All new drugs are required to comply with the provisions and requirements of Schedule Y of the Drugs and Cosmetics Act for registration in India. However, some relaxations have been granted for FDCs to be registered in India. For this purpose, FDCs are categorised into the following four groups:

(i) The first group of FDCs includes those in which one or more of the active ingredients is a new drug. Such FDCs are treated in the same way as any other new drug, for both clinical trials and marketing permission.

(ii) The second group of FDCs includes those in which the active ingredients are already approved and marketed individually but are combined for the first time, for a particular claim and where the ingredients are likely to have significant interaction of a pharmacodynamic or pharmacokinetic nature.

In order to obtain permission to carry out clinical trials with such FDCs, a summary of available pharmacological, toxicological and clinical data on the individual ingredients should be submitted,

along with the rationale for combining them in the proposed ratio. In addition, acute toxicity data (LD 50) and pharmacological data should also be submitted on the individual ingredients as well as their combination in the proposed ratio. If clinical trials have been carried out with the FDC in other countries, reports of such trials should be submitted. If the FDC is marketed abroad, the regulatory trials performed should be stated. For marketing permission, the reports of clinical trials carried out with the FDC in India should be submitted. The nature of the trials depends on the claims to be made and the data already available.

(iii) The third group of FDCs includes those that have received marketing approval, but in which it is proposed either to change the ratio of active ingredients or to make a new therapeutic claim. For such FDCs, the therapeutic rationale should be submitted to obtain permission for clinical trials and the reports of trials should be submitted to obtain marketing permission. The nature of the trials will depend on the claims to be made and the data already available.

(iv) The fourth group of FDCs includes those whose individual active ingredients have been widely used for a particular indication for years, their concomitant use is often necessary and no claim is proposed to be made other than convenience.

In determining whether it is rational to combine actives into a single product, there are medical, quality and bioavailability considerations:

(i) Quality issues may be addressed by much the same criteria that apply to single-component products and it is difficult to imagine a case in which essentially the same standards would not apply.

(ii) Medical considerations are more complex and sometimes contradictory, for example, when increased efficacy is accompanied by increased toxicity. The decision as to whether to give marketing approval for a new FDC is often based on a consideration of the balance of advantages and disadvantages from the medical perspective.

(iii) Interpretation of the results of bioavailability and bioequivalence tests involves both quality and medical considerations. For example, it is not acceptable that bioavailability is reduced or variable when compared with single-entity products because of poor formulation, but an interaction between two active pharmaceutical ingredient (APIs) that leads to an increased bioavailability may be one of the advantages taken into account when balancing the pros and cons of introduction.

All the potential limitations and advantages of the combination are expected to be listed and discussed while providing a licence to the product. The discussion should be based on the available data and on scientific and medical principles. However, drugs controllers hardly take into consideration the scientific basis of combining more than one drug. Also, existing provisions in the Drugs and Cosmetics Rules are considered insufficient to ensure scientific evidence before approving any FDC. In India, if an FDC is approved in any state, the same could be marketed throughout the country. The company does not require any clearance from any other state where it is being marketed. Taking cognisance of the flooding of the market with irrational FDCs, the DCGI has directed all state drugs controllers to take necessary action with respect to FDCs vide letter no. F. No. 19013A/2007-D dated August 14, 2007. It included the list of 1,000-plus FDCs not permitted by the DCGI but permitted by state drug regulators. In September 2007, the DCGI circulated a notification declaring 294 FDCs as irrational. The Confederation of Indian Pharmaceutical Industries moved the Madras High Court and received a stay order on the DCGI directive against the 294 FDC drugs, which had been categorised as 'absurd,' 'rejected,' banned and under examination.

Drug Promotion

The Drugs and Magic Remedies (Objectionable Advertisements) Act, 1954, lists disease categories for which advertisements cannot target consumers directly. However, advertising to a registered medical practitioner is permitted if it is carried out in a confidential manner according to the Act. It has been reported that the industry

spends on average nearly 20 per cent of sales turnover, or in real terms ₹ 5,000 crore, for sales promotion while the average expenditure on research and development in India is only around 4 per cent.

Certain industry organisations have prepared code of conduct for promotion and marketing, but it is inadequate and provide no or insignificant measures against violation. The Organisation of Pharmaceutical Producers of India has also come up with a Voluntary Code on Marketing Practices which calls for maintaining strict ethical standards, i.e., no financial benefit or benefit in kind should have an inappropriate influence on the professional's prescribing practices. However, evidence suggests otherwise, as firms sometimes engage in aggressive marketing tactics, including showering physicians, pharmacists and wholesale distributors with expensive gifts (Roy, Madhiwalla *et al.,* 2007). Another major issue is the possibility that drugs are prescribed or dispensed more for the financial interests of the prescribers and dispensers than for the needs of the patient. Also, while the code of conduct of the Indian Medical Council insists that doctors make prescriptions in generic names, there is little monitoring of its implementation. The need of the hour is enforcement of strict controls on marketing by the government regulatory agencies. Recently, the DoP came out with detailed guidelines on a voluntary code of conduct against the unethical promotion strategies of the pharmaceutical industry.

Consumer Information

The pharmaceutical sector is unique when it comes to product consumption, as the choice is made not by the patient but by the doctor prescribing medication. In India, people mainly depend on doctors and pharmacists to provide drug information but they often fail to do so. Currently, there is no single source or database dealing exclusively with consumer drug information. Moreover, adequate and necessary information is not being disseminated in local languages. In the absence of accurate and reliable information, consumers/patients in India fail to exercise choice. This asymmetry in information in turn compromises competition in the pharmaceutical market. It is recommended that

a comprehensive database of drug information be developed by the government as a source of reliable and accurate information for consumers. Such a database should be made publicly available, including on the Internet.

Conclusion

To sum up, the principal objective of drug regulation in India, especially the agencies involved in drug regulation, whether it is the CDSCO or the DoP, till now appears to be promotion of the industry; their activities are directed to meeting the aspirations and demands of the industry. On the other hand, the mission and goals of any drug regulatory system must be aimed at meeting the aspirations of the people and public health interests, such as safety, efficacy and cost-effective solutions involving medicines and medical devices. Unless and until this is recognised and promoted by the regulatory institutions, public health goals will continue to be accorded only secondary importance in the country.

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10

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Conclusion and Future Policy Directions

Despite being the 'pharmacy of the global south,' access to medicines for a large majority of Indians is impeded by both physical and financial reasons. Currently, the Indian pharmaceutical industry not only produces adequate quantities of drugs but almost 40 per cent of what is produced in the country is exported to other countries. Due to continued neglect and underinvestment in public health system, access to medicines in public health facilities has suffered in the past and especially so in the last two decades. Specifically, fund allocation to procure drugs in public health system has been extremely limited, where, except Tamil Nadu and Kerala and few other states, past experience in most Indian states suggests that it has been less than five per cent of overall public health expenditure. Further, poor governance and weak accountability were also equally responsible for a sorry state of affairs. Since the government, both central and state, had allocated limited budget to procure drugs and a sustained neglect of public health facilities, households are exposed to open market purchases, whereby it is now estimated that nearly 70 per cent of all households spending on health care is on buying medicines.

Adding to this woeful scenario, direct price control on medicines, which had been the hallmark of late 1970s and 1980s, gave way to liberalisation of the sector, leading to a scenario where nearly 90 per cent of the medicine market is not price controlled now. This problem was exacerbated recently due to exorbitant price charged on patented medicines, as India had moved to a product patent system in 2005. Promoting access to medicines is further eroded due to serious threat of irrational use of medicines. Not only hazardous

and inessential medicines are sold in the country but irrational prescription, dispensing and use of drugs are rampant in India. The regulatory oversight to control and implement legislations is weak and poorly implemented. In order to remove these impediments and to provide universal access to essential medicines, a recent report of High Level Expert Group (HLEG) of the Planning Commission, calls for meeting these goals through four principles of 'universality, equity, efficiency and quality.' We outline here few specific policy options available before the government for accelerating and achieving universal access to essential medicines in India.

Accelerate Government Expenditure on Drug Procurement to 0.5 per cent of the GDP

Currently, the Indian government, both central and states, put together, incurs approximately ₹ 6,000 crore (0.1% of GDP) for procuring medicines. The HLEG estimated that an additional four to five times increase in government drug procurement would be needed at ₹ 24,000 crore (0.4% of GDP). Together, this is estimated to cost roughly ₹ 30,000 crore (0.5% of GDP), approximately half a per cent of GDP. Such an enhanced outlay is expected to lead to supply of generic drugs to everyone visiting public health facilities and private health care system which are contracted into the UHC (Universal Health Care) system. As far as public health system is concerned, supplies of quality generic medicines could be ensured through a pooled public procurement. We argue that in addition, expanding Jan Aushadi Stores (JAS) to cover patients who access private health facilities under UHC will achieve substantial gains in access to essential medicines.

Strengthen Drug Procurement and Distribution System in Central and State Governments

- Implement a centralised procurement and decentralised distribution model. In order to procure drugs, vaccines and medical devices, we recommend that both the central and state governments establish and implement a procurement and distribution model based on TNMSC (Tamil Nadu Medical Services Corporation). This model which has

been adopted in the neighbouring Kerala and recently in Rajasthan, has received desired attention and needs replication in other states. Public health system in the country needs to move away from the fragmented, decentralised procurement model to a centralised system, where by utilising the monopsony power of the government purchaser, medical products can be procured at rock bottom prices from the manufacturers directly. Thus, economies of scale could be achieved using monopsony power of larger government purchaser.

This type of system is expected to broadly improve governance, accountability and transparency in the government procurement and distribution system. The TNMSC system allows for a two-bid tendering model, whereby technical and financial bid is invited from the drug makers in order to ensure quality and cost-effective solution. The drugs to be procured under this system will encourage purchase of quality, generic and essential medicines. As far as distribution of essential medicines in the public health system is concerned, there is a need to establish one warehouse in each district, which must be effectively linked to the public health facilities and the central procurement agency. This is expected to efficiently and effectively deliver drugs and vaccines in the front-line government health facilities. Ultimately, the objectives of delivering drugs without acute shortages and chronic stock-outs would be achieved.

- Recognising the fact that the current outpatient care and drugs purchased by the households still predominantly occurs at the private health facilities/chemists, the government is required to strategically engage the current JAS. The Department of Pharmaceuticals (DoP) which has established and is operating the JAS needs to expand and extend the stores in districts and areas that are unreached by the private chemists. Such stores may be established in at least one at every block level and four to five at district headquarters. Medicines and vaccines supply to such stores

would be linked to centralised procurement at state level. This mechanism will result in greater monopsony power leading to cost-effective solutions and rational use of medicines.

- While allopathic medicines are critical in the public health system, the government also needs to seriously consider, including AYUSH, medicines and procure them and distribute in similar fashion as in allopathic drugs. This would mean identifying and approving chemical, biological and traditional Indian medicines or AYUSH medicines, which would be centrally procured and distributed in a decentralised level.

Enforce Price Control on All Essential Drugs based on Cost-based Pricing Mechanism

Since nearly 70 per cent of all outpatient care and drugs are procured by the households from the private health facilities, and given the substantial expenses incurred by households, the government is required to bring all 348 essential drugs under direct price control. Although the current NLEM (National List of Essential Medicines, 2011) covers most therapeutic categories, there are still a large number of them which are typically essential and life saving, which needs to be considered while applying price control. Moreover, the dosages and strengths mentioned in the NLEM may not adequately cover substantial range of medicines. Therefore, all dosages and strengths mentioned under NLEM must be brought under the price control. Further, NLEM drugs and its therapeutically equivalents must also be under price caps. This is critical due to the fact that not only several 'me too' drugs pushed into the system by the drug makers which are considered therapeutically equivalent but also a substantial share of the drug market is flooded by fixed dose combinations (FDCs). If FDCs relating to NLEM are left out of price control, drug manufacturers would simply wriggle out of price control by producing and pushing such FDCs in the market.

But a more contentious and a vexed issue is to do with the mechanism of price control. The current price control mechanism is based on cost-plus-based pricing (CBP) which has been followed

since 1979. The National Pharmaceutical Pricing Policy, 2011 (NPPP, 2011), calls for moving away from cost-based pricing to market-based pricing (MBP). Several mechanisms are being floated by the government based on MBP, such as, (i) price ceiling based on top three brands in each medicine market; (ii) median price of medicines; (iii) price ceiling based on weighted average price (WAP) of brands with one percentage market share by volume. This new set of market-based mechanism is only expected to sharpen the price rise and legitimise sky-high drug prices. Therefore, we call for the continuation of CBP mechanism on all essential drugs. This would also mean plugging all loopholes of escape routes so that drug makers do not wriggle out of price caps.

In addition, the DoP must be required to continuously collect and disseminate pharmaceutical market data, such as market share, consumption pattern and prices, which are currently being done by a private data collecting agency (like IMS Health). The prohibitive cost of obtaining this data from a private agency makes independent evaluation by health and public interest groups an impossible task. Such data should be available in the public domain, and it is well within the powers of the government under the Essential Commodities Act to gather and disseminate such data.

Building Public Sector Capacity and Protecting the Capacity of Indian Private Sector Companies to Produce Low-cost Drugs and Vaccines

It is ironic that despite India supplying quality generic drugs around the world, the country has concerns about sufficient domestic drug supply and vaccine security. With the increasing acquisition of Indian companies by transnational drug corporations, there is a pressing need to rethink our country's drug strategy. Even when multi-national drug firms are not acquiring Indian-owned drug manufacturing companies, effective control on policies and pricing may be gained through 'strategic alliance' agreements. Various options are proposed below for the government's consideration. (i) In order to reduce our vulnerability to restructuring and its serious implications, we suggest that the government strengthen public sector units (PSUs), which have drug manufacturing capability. This

is possible through infusion of capital into existing but 'sick' PSUs such as Indian Drugs and Pharmaceuticals, Ltd. (IDPL), Hindustan Antibiotics Limited (HAL), and state-owned enterprises, in addition to providing them with autonomous status. (ii) The use of PSUs will offer an opportunity to produce drug volumes for use in primary and secondary care facilities as well as help in 'benchmarking' drug costs. The existence of PSUs would also provide an opportunity to utilise the provision of compulsory licensing (CL) under Trade Related Aspects of Intellectual Property Rights (TRIPS). (iii) In addition, we also need to urgently revisit India's FDI regulations to amend the present rules of an automatic route of 100 per cent share of foreign players in the Indian industry to less than 49 per cent, so as to retain predominance of Indian pharmaceutical companies and preserve our self-sufficiency in drug production. Another option is to move the drug industry from an automatic route to the Foreign Investment Promotion Board (FIPB) route, which would ensure that all proposals of foreign mergers and acquisitions of Indian drug companies are scrutinised thoroughly. Alternatively, a provision for separation of 'financial' ownership from 'legal' ownership may be enforced, analogous to the Reserve Bank of India (RBI) rules, which limit the voting rights of the foreign investor. (iv) The domestic drug manufacturing industry should transition from the current scenario of import dependency to self-sufficiency with respect to ingredients. The active pharmaceutical ingredients (APIs) industry has placed the drug-making (formulation) sector in jeopardy in recent years. India, which was to a large extent self-sufficient in API manufacturing until the 1990s, has found itself in an awkward position in recent times with several disruptions and cost-escalation of largely Chinese imports. There is a need to incentivise domestic production of APIs in the private sector, while at the same time actively engage drug PSUs to manufacture quality and cost-effective APIs. (v) There is also a need to engage medium and small-scale drug industries in the production of quality generic medicines for UHC by helping them to transit to Good Manufacturing Practice (GMP)-compliant status, by providing financial and non-financial assistance. (vi) Vaccine security is equally vital given the large disruption that the country experienced in vaccine supply recently. In view of this, we suggest that existing public sector

vaccine-manufacturing units be strengthened with additional infusion of capital and the provision of autonomous status, and new vaccine parks be set up immediately. Indian private sector units manufacturing vaccines must be safeguarded against external interference with their mandate to prioritise Indian needs, as in the case of drugs.

Promote Rational Use of Drugs through Prescriber, Patient and Public Education

- There is a clear need to phase out hazardous, non-essential and irrational medicines, and irrational 'fixed dose drug combinations' from the market. Recent reports on 'superbug' nosocomial infections, indicative of anti-microbial drug resistance in India, clearly point to the need to end the irrational drug prescription and dispensing practices.
- Efforts will need to be backed by education and behaviour change among doctors, towards the adoption of rational prescribing and dispensing procedures for drugs, possibly through the advocacy of national and state health promotion trusts.
- Standard Treatment Guidelines (STGs) should be implemented in the national health policy (NHP) system and should include only rational formulations.
- Unethical or aggressive marketing practices by drug and devices manufacturers and sales persons as well as incentives offered to doctors to promote prescriptions should be banned and penalised.

Strengthen Central and State Regulatory Agencies to Effectively Perform Quality and Price Control Functions

- Regulatory mechanisms need to be tightened for better drug quality control. Existing state regulatory agencies in India do not have an adequate workforce or appropriate testing facilities. Fresh investments have to be made for setting up regulatory facilities in each state and recruiting

additional regulators, which is absolutely essential for regulating manufacturing drug units as well as drug outlets.

- Global practices in drug regulation involve a variety of functions and mechanisms that range from food control, drug quality and safety, pharmaceutical price regulation and medical devices, and equipment standardisation. The problem in India is that while only some of these functions are undertaken by the Central Drugs and Standard Control Organisation (CDSCO), there are multiple additional authorities and departments that fail to coordinate among themselves for efficient and effective functioning. For instance, the DoP under the Ministry of Chemicals and Fertilisers is responsible for drug price control, while the Essential Drug List (EDL) is prepared by the Ministry of Health and Family Welfare. Therefore, there is a need to integrate the role of drug price control into the CDSCO. In addition, the CDSCO should have responsibility for collecting, tabulating and disseminating data on drug production, category-wise sales, company level information on drugs and undertake the responsibility of carrying out prescription audits. Currently, various ministries rely on private data on drug consumption (which is both expensively priced and whose methodology is not very robust) to formulate drug price policies. To make the policy-exercise more credible and authentic, the Health Ministry must be empowered to take necessary action in this direction.
- Adding new drugs and vaccines to the government drug procurement system must be based on scientific evidence, with due regard to safety, efficacy and cost. We propose an institute akin to the National Institute for Clinical Excellence (NICE) in the United Kingdom to critically evaluate the evidence needed to guide decisions on inclusion of new drugs and vaccines into the public health system.

Protect the Safeguards Provided by the Indian Patents Law and the TRIPS Agreement against the Country's Ability to Produce Essential Drugs

- India's current amended patent law includes several key safeguards such as restriction on the patenting of insignificant or minor improvements of known medicines (under Section 3[d]); this provision needs to be protected from any dilution.
- Secondly, CL should be issued to companies, as necessary, to make available at affordable prices all essential drugs relevant to India's disease profile. This provision, under India's own Patents Act and TRIPS as clarified by the Doha Declaration, allows countries to use such licences in public interest and can be invoked in the interest of public health security.
- Finally, the 'data exclusivity clause' must be removed from any free trade agreement (FTA) that India enters into, since such a clause extends patent life through 'evergreening' and adversely affects drug access and affordability.

Transfer the Department of Pharmaceuticals to the Ministry of Health

The manufacture of drugs is under the purview of the DoP, which is presently a part of the Ministry of Chemicals and Fertilisers. This department is also responsible for drug price control. Since the Ministry of Health is not only responsible for ensuring the quality, safety and efficacy of drugs but is also accountable for the unhindered availability of all essential drugs in the UHC system, public interest would be best served by transferring the DoP to the Ministry of Health. This would help to better align drug production and pricing policies to prioritise national health needs.

Expected Outcomes

We believe that our recommendations could tremendously improve and enhance physical and financial access to medicines

in the country in a short span of time. Overall governance and accountability of both public and private players involved in drug procurement, distribution, financial allocation, and drug quality requirements should improve. This is likely to be reflected in regular availability of all essential medicines and elimination of drug stock-outs. Other key outcomes as a result of these recommendations will include:

- Scaling up public spending on health and allocating at least 15 per cent of that funding for drugs is expected to dramatically reduce out-of-pocket (OOP) spending for households. The adverse ratio of government to households on drug spending which is presently at 1:10 is likely to be reversed or at least substantially reduced.
- Significant reduction in impoverishment and catastrophic spending due to OOP expenditure on drugs.
- A centralised drug procurement and decentralised distribution mechanism would produce much needed economies of scale through monopsony purchasing, significantly reducing drug prices and creating better value for money. This system can be further strengthened by allowing the purchase of only generic drugs from the essential drug list. Since physicians in the public health facilities would be required to prescribe only EDL drugs and follow STGs, rational prescription and dispensing would increase.
- Bringing all essential medicines under price control would have a beneficial effect on open market drug prices, resulting in large savings to households.
- Strengthening drug control institutions and staffing drug control authorities with a skilled workforce will reduce the production and sale of spurious and sub-standard drugs, and increase the confidence of the Indian public in drug quality.

11

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Post Script

Pharmaceutical policy landscape is a dynamic one which requires concerted and collective response. We began this exercise in the year 2008 but in the process, several policy changes have occurred, especially in the last two years (2011-2013). This post-script is a response to assess the policy changes and its implications for access to essential medicines. We outline the features of three sets of policy changes and assess its implications including: price ceiling, product patents and investment in the pharmaceutical sector.

On Drug Price Ceilings

For nearly last 10 years, the Government of India (GoI) was attempting to formulate its strategy to control essential drug prices. Despite one task force report (Pronab Sen Report, 2005), two consecutive empowered Group of Ministers (GoM) and a draft policy [National Pharmaceutical Pricing Policy (NPPP), 2011/12], the government finally notified Drug Policy Control Order (DPCO) in 2013. This was made possible by a steady nudging from the Supreme Court which directed the GoI to bring all key essential drugs under price control. Prior to the notification of DPCO, 2013, the Ministry of Health and Family Welfare (MoHFW) had brought out a latest version of National List of Essential Medicines (NLEM) in 2011. The Department of Pharmaceuticals (DoP), under the Ministry of Chemicals and Fertilisers, later circulated the NPPP, 2012.

Several methods were floated for fixing ceiling prices for essential medicines. The NPPP 2012 called for moving away from the past practice of cost-plus-based pricing (CBP) to market-based pricing (MBP) for 348 essential medicines under 'price control.'

While CBP basically allowed manufacturers to charge a profit over the cost of production, the current method of MBP is based on the simple average price of brands with 1 per cent share by value. The 1 per cent cut-off was intended to ward off non-serious players from the market and calculate the price ceiling from the rest. In a sector that is characterised by 'supplier-induced demand' and a market peculiar for 'market-leader is price-leader' syndrome, any formula based on MBP is expected to officially legitimise unaffordable drug prices. The approach is problematic because it covers merely 18 per cent of the total market for drugs in India. The whole exercise was like chasing a mirage of an elusive formula to balance the interests of producers and patients, but mostly the only consistent direction that the policy was pursuing from day one was to somehow keep the interests of the pharmaceutical industry a priority. Ultimately, the drug makers benefited from a policy muddle that was directionless.

Further, the Drug (Price Control) Order 2013 (DPCO, 2013) does not cover combinations of essential medicines other than the few that are on the NLEM, and is strictly restricted to the dosages and strengths listed in the NLEM. Combination products not coming under price control accounted for 45 per cent of the total market value in 2012 (₹ 33,118 crore). Moreover, of the top 20 brands introduced in the past 24 months, a majority (18) fall outside price control. Given that the primary objective of price control is to contain the high prices of medicines, the scope of DPCO 2013 will not extend to new market entrants. Of the 390 formulations for which prices have been notified, in 370 cases (95%), the market leader by sales is observed to hold a high market share (i.e., 25% or greater). Based on calculations using the National Pharmaceutical Pricing Authority (NPPA) data, the price of the market leader will not be reduced in 104 cases (27%) and only a limited reduction (i.e., 10% or less) in the price of the sales leader will be seen in another 64 cases (16%). Far lesser impact on the prices of market leaders is seen in the case of a number of formulations used as anaesthetics, antidotes and other substances used in poisoning, anti-migraine medicines, immunologicals and electrolyte disturbance.

Contrary to the claim that MBP will be 'based on widely available information in the public domain' and lead to more 'transparent and fair pricing,' the government is relying on commercial data from IMS Health that are neither available for public scrutiny nor easily accessible due to the high cost of the database. Moreover, the government has recently admitted that it is bound by legal obligations 'as per memorandum of understanding with IMS Health' that prevents sharing of the data with third parties. The government has depended heavily on the expertise and data provided by IMS Health without any means to assess its quality, limitations or biases of the data. Because market estimates are entirely modelled based on the results of primary surveys of prices, the methodology and survey sample can significantly influence the market data. In fact, we have observed several cases where the market estimates can vary quite widely between IMS Health and another independent source of market-based data. Moreover, data for more than 20 per cent of the formulations for which NPPA is charged with fixing price ceilings are missing in the IMS database. The government's use of proprietary data, about which no details are available to the public, to set national policy is a concern.

The main problem with DPCO 2013 is that it makes the interests of the ₹1 trillion industry a priority, while patients' interests in particular and the larger public health goals are secondary. Direct drug price control, which was a key component of any pharmaceutical policy in the past, is now officially buried. This was gradually dismantled; from covering nearly 90 per cent of the drug market in the late 1970s, the percentage of the medicines market that was controlled until DPCO 2013 was notified stood at around 10 per cent. With the new policy, the pretence of drug price control is now completely dismantled. By excluding fixed dose combinations (FDCs) involving essential medicines from price control, and by restricting itself only to the dosages and strengths of medicines listed in NLEM, the new policy appears to be designed for the pharmaceutical industry to have ample room to wriggle out of price control in the future. To top the agenda of pharmaceutical industry interests, the policy is designed to allow drug makers to raise the price of unscheduled formulations by up to 10 per cent

annually. It is interesting to observe that India's long-term average price increase annually is in the range of 7-8 per cent, while the new drug policy showers goodies on the industry by allowing a liberal 10 per cent price rise per annum.

On Foreign Investment

India opened up its door for foreign investment in the pharmaceutical industry in the late 1990s. This included 100 per cent foreign direct investment (FDI), although the pharmaceutical sector has been attracting relatively less foreign investment in the past (a long-term average investment of less than 2 per cent over the last two decades). However, a spate of takeovers of Indian drug companies by foreign multinationals has caused concerns of such investments. Evidence suggests that over 98 per cent of all such foreign investments in India in the last 6-7 years have been in the Brownfield investment category and not greenfield category.

While greenfield investment is considered desirable, several concerns about implications of brownfield investment ranges from drug insecurity to distortions in production pattern, reduced market share and a subsequent loss of competitive edge, leading to drug price rise. Any investment, especially foreign investments, must be guided by the following broad principles: (i) any new investment must bring in new technology (technology transfer), deepen research and development activities, and augment local production capacities, (ii) create infrastructure in the pharmaceutical sector besides adding new jobs; and (iii) investment must be channeled in desired direction so that inadequacy in several therapeutic segments can be addressed.

Although FDI of the brownfield category is allowed, the flow of such investments is currently conditioned on the following criteria: (i) production of any drug on NLEM must be continued for at least five years even after acquisition of Indian companies by foreign multinationals corporations (MNCs); (ii) foreign companies acquiring Indian pharmaceutical companies must maintain the level of current expenditure on research & development (R&D) for at least three subsequent years; and (iii) foreign companies must ensure that when such takeovers occur, they bring in new technology, not available with the Indian players. Despite the

best intentions of invoking such conditionalities, the spate of acquisitions continues to occur to the detriment of domestic drug industry leading to intensification of drug insecurity in the country.

(i) According to Department of Industrial Policy and Promotions's (DIPP's) data on FDI, the pharmaceutical sector ranked fifth in sector-wise FDI equity inflows for the period April 2000 to June 2013 and accounted for 5.7 per cent of the total FDI inflows. However, foreign investment in this sector has intensified in recent years. FDI inflows for the pharmaceutical sector for the period April 2011 to June 2013 account for about 48 per cent of the total foreign investment inflows for the period April 2000 to June 2013, according to reported data.

(ii) MNC's share in the Indian pharmaceutical market of approximately ₹ 70,000 crore was 29 per cent in 2012 (see Annexure Table A-11.1), while the market share of the top 10 Indian companies was 32 per cent.

(iii) In fact, the share of MNCs in the top 20 companies has increased from 14.4 per cent in 2005 to 21.6 per cent in 2012. Whereas only one MNC was ranked among the top 5 companies (by sales) in 2005, 3 MNCs were among the top 5 companies in 2012.

(iv) Acquisitions have led to growing control of MNCs on the Indian pharmaceutical market. Abbott is a case in point. Its rank went up from 14 (2% market share) in 2005 to the company with highest market share in 2012 (7.1%) after its takeover of Piramal Healthcare's generics business unit in 2010 (Piramal ranked number 4 with a market share of 4.6% in 2005; see Annexure Table A-11.2).

(v) The Indian pharmaceutical market is characterised by significant market concentration in several therapeutic segments. Some of the segments of public health relevance have a high concentration with four firms capturing 80-100 per cent of the total market share (Annexure Table A-11.3). These include segments in vaccines, human insulin, oncology and cardiovascular care. In addition, numerous

segments that also have high public health importance demonstrate moderate concentration such as antiepileptics, antibiotics, antipsychotics, etc. (Annexure Table A-11.4). Further consolidation in any of these segments could pose a threat to competitiveness and patient affordability.

The current conditions under the Foreign Investment Promotion Board (FIPB) route do not provide adequate basis to evaluating proposed investments against public health concerns. Rather they reflect an *ex post* set of criteria without any mechanism for monitoring or enforcement.

Therefore, there is an urgent need to revisit the current conditionalities and revise the FDI policy. Any new conditions must be based on the principles of objectivity, transparent and be measurable. In order for the country to benefit from foreign investment, the following conditions must be made mandatory:

(i) Future investment in pharmaceutical brownfield should remain outside the 'automatic' route.

(ii) A case-by-case approach must be followed in vetting each proposal for brownfield investment which takes into consideration all aspects that could impact on health security. Specific obligations must be defined for each case in granting the clearance.

(iii) Investors must be required to bring in matching grants of equal proportions to the value of the investment. The matching grant must be required to be invested in augmenting/expanding production capacities and R&D activities. The matching grants must be allowed to be deposited in escrow account to be monitored continuously by the Reserve Bank of India (RBI). And this must be ensured to flow into the company within two years of initial investment and takeover of Indian company.

(iv) Obligations for local manufacturing of finished products and investment in API production should be imposed.

(v) The ramifications of allowing further FDI in several therapeutic segments where the current market reflects a

monopoly/oligopoly scenario, where few players exist, are considerable. Brownfield investment in these markets with high public health significance should be disallowed as a matter of safeguarding health. In several verticals, where the current market reflects a monopoly/oligopoly scenario, where very few players exist, brownfield investment must be disallowed. And this list would include vaccines market, injectibles, API, rifampicin, erythromycin, ARVs, oncology market, biosimilars, etc. However, given the dynamics of the pharmaceutical market, these categories would undergo substantial changes with time, and therefore, there is a need to revise such a negative list of verticals.

(vi) A stringent monitoring mechanism to determine non-compliance with obligations and conditions should be put in place which may include monitoring of prices, substitution and changes in product mix, quantity and nature of investments in R&D and manufacturing, quantity of imports of finished good, etc.

On Pharmaceutical Patents

In 2005, India signed the WTO (World Trade Organization)-TRIPS (Trade-Related Aspects of Intellectual- Property Rights) agreement and moved to from process to product patent system of pharmaceutical products. The former, which existed from 1970 to 2004, allowed domestic firms to innovate and produce low-cost generic versions of patented medicines. Under the post-2005 system, multinational drug makers with new inventions are allowed market exclusivity for 20 years from the date of filing of patent application. This prevents generic drug makers from innovating and producing low-cost generic versions for 20 years.

The rejection of the Novartis petition challenging one of the most progressive tenets of the Indian Patents Act (1970), as amended in 2005 by the Supreme Court, is a landmark verdict for the public health community and the generic drugs industry, in particular, and for global health. Under the amended Indian Patents Act, Section 3(d) allows drug companies to obtain product patents for new salts or chemical ingredients. This is intended to encourage

drug companies to protect their rights and prevent these from being copied by competitors, allowing for a 20-year protection period to recoup investments. However, Section 3(d) does not encourage frivolous patents. It is intended to encourage only breakthrough innovations and discourage new use of known chemical substances or new delivery mechanisms of existing chemical compounds.

Transnational drug companies not only possess the first mover advantage, but owing to the high-voltage brand image they create, often extend their patents well beyond the already long period of protection. Drug companies are known for 'evergreening' patents by filing new patents, tweaking existing molecules to show novelty. Innovation is a red-herring, often used by multinational drug companies to make super-profits at the expense of social good and well-being. Under the mailbox agreement of TRIPS provisions, India received over 9,000 mailbox applications as patent filings post-2000, while a major share of those were for pharmaceutical patents. Global evidence, on the other hand, shows that roughly 275 such patents were filed and granted for blockbuster drugs during this period. In order to pre-empt Indian generics companies from producing these drugs and to keep them away from the market, the big pharma companies have flooded the patent offices with frivolous patent applications, known to be existing molecules tweaked to appear as a novel product.

The R&D Myth

The night before the apex court verdict, Novartis threatened to stop investing in R&D in India, if the verdict went against it. How serious is the threat and how realistic the scenario? In India's drug production of over ₹ 100,000 crore, Novartis' turnover is a little over ₹ 1,000 crore, constituting around one per cent. Out of the total expenditure of over ₹ 800 crores incurred by Novartis India in 2012, a paltry ₹ 29 lakh was for R&D, constituting roughly 0.03 per cent of its entire expenditure in India.

Can such low spending can be considered R&D investment? In fact, Novartis R&D expenditure in India for the past five years has been in a similar range. On the other hand, Novartis consistently posted a profitability ratio (profit after tax as percentage of total

income) of over 15 per cent in the last five years, something to envy for other sectors.

Big Pharma argues that if global R&D of innovator companies were to be considered, transnational drug corporations spend over US $1 billion to come up with a new drug. This includes cost of R&D incurred on failed drugs as well, as pharmaceutical companies take, on an average, roughly 12-13 years to get patents on new drugs. The magic $1 billion figure is a gross overestimate. Even by conservative calculations, this figure would be one-fifth or one-fourth of the billion dollar estimate. But Big Pharma is quick to recoup its R&D spending from blockbuster drugs. Take the case of Gleevec (ImatinibMesylate), sold in the US. Novartis raked in a total turnover of $1.69 billion from the US alone in 2012 from the drug. The global turnover on Gleevec is anybody's guess. It is also widely known that the cost of manufacturing drugs is only a fraction of the turnover.

Novartis currently sells Glivec (Gleevec) for ₹ 4,115 per tablet, while Resonance, an Indian generic drug company, dispenses it at ₹ 30 per tablet. The annual cost of treatment per patient on Glivec would be in the range of ₹ 15 lakhs, while Indian generic companies are offering it at ₹ 10,000. If Novartis were to get its patent on Glivec, Indian generic companies would have to stop their production, and therefore an unaffordable scenario would have prevailed for the common man in not only India but in other developing countries. Thankfully, the court ruled in favour of Section 3(d) of the Patent Act.

Novartis claims that 95 per cent of cancer patients in India were provided the medicine free. This is patent untruth. Retail market sales in India for Glivec, sold by Indian generics producers, are currently worth ₹ 20 crores. Novartis sells Glivec directly to patients and not through the usual retail chain, a system that is designed to make people believe that they offer the drug free.

After seven years of battle, the Supreme Court verdict seals this issue, facilitating patent controllers to strictly enforce Section 3(d), thereby pre-empting pharmaceutical companies that seek to evergreen products. However, there are several other safeguards that

are enshrined in the patent law that must be utilised to make life-saving and essential drugs affordable. And one such key safeguard is invoking compulsory licensing (CL) for blockbuster drugs, if the original manufacturer fails to sell it at affordable rates.

A CL is issued by the government to authorise the procurement, import, manufacture and marketing of an affordable generic version of the expensive patented medicine on the payment of a royalty to the patent holder. This is done to make medicines affordable. Thus, CLs can be issued to generic producers if patented drugs are unavailable or unaffordable domestically or if countries that lack production capacity order drugs from India. The government can also notify drugs on which CLs are needed for public non-commercial use and in situations of national emergency or extreme urgency.

India's first CL was notified seven years after the implementation of the TRIPS agreement and was initiated not by the government but by an application made by a generic manufacturer—Natco—before the Indian Patent Controller. Bayer obtained patent and marketing rights in India for Nexavar, a drug used in advanced kidney and liver cancer in 2008. Bayer priced it at ₹ 2.8 lakh per patient per month. Cipla entered the market in 2010, launching sorafenib tosylate, charging ₹ 30,000 per patient per month for the drug.

In 2011, Natco started CL proceedings by applying first for a voluntary license from Bayer and then following it up with an application before the patent controller. Offering to market the drug at ₹ 8,800 per person per month, Natco received the first CL in March 2012, against the payment to Bayer a 6 per cent royalty on sales.

Immediately after the CL was issued to Natco, Cipla went into the market by dropping its price further to ₹ 6,840. While Cipla is facing infringement suit from Bayer for violating patent law, Natco's case was challenged by Bayer in Intellectual Property Appellate Board. But Natco was granted the CL because the Bayer had made the drug only available to a small percentage of patients (approximately above 2%), which did not meet the requirements of the public interest. The Intellectual Property Appellate Board had only upheld Natco's claim for CL and dismissed Bayer's petition.

Annexure Table A-11.1

Market Share of Indian Companies and MNCs in the Indian Domestic Pharmaceutical Market

	2012 Sales (₹ crore)	*Market Share (%)*
Indian	50,706.21	71
MNC	20,539.80	29
Total market	71,246.01	100

Source: IMS Health.

Annexure Table A-11.2

Share of Top 20 Indian and MNCs in Indian Pharmaceutical Market, 2005 and 2012

	2005*				2012*		
Company Rank	*Company Name*	*Sales (₹ in crore)*	*Market Share (%)*	*Domestic/ MNC*	*Company Name*	*Sales (₹ in crore)*	*Market Share (%)*	*Domestic/ MNC*
1.	Glaxosmithkline	1339.68	5.8	MNC	Abbott	506.25	7.1	MNC
2.	Cipla	1185.27	5.1	Indian	Cipla	3542.67	5.0	Indian
3.	Ranbaxy	1158.38	5.0	Indian	Sun	3067.83	4.3	Indian
4.	Piramal Healthcare	1062.11	4.6	Indian	Ranbaxy	3008.69	4.2	MNC
5.	Zydus Cadila	864.34	3.7	Indian	Glaxo-smithkline	3004.72	4.2	MNC
6.	Sun Pharma	754.81	3.2	Indian	Zydus Cadila	2841.89	4.0	Indian
7.	Alkem	686.37	3.0	Indian	Mankind	2437.12	3.4	Indian
8.	Pfizer	563.27	2.4	MNC	Alkem	2365.46	3.3	Indian
9.	Sanofi Aventis	560.99	2.4	MNC	Pfizer	2287.03	3.2	MNC
10.	Aristo Pharma	543.11	2.3	Indian	Sanofi	2034.87	2.9	MNC
11.	Dr. Reddys Labs	541.68	2.3	Indian	Lupin Ltd.	2003.58	2.8	Indian
12.	Alembic	521.25	2.2	Indian	Macleods Pharma	1970.64	2.8	Indian
13.	Lupin Labs	513.81	2.2	Indian	Intas Pharma	1765.34	2.5	Indian
14.	Abbott	480.88	2.1	MNC	Emcure	1571.74	2.2	Indian
15.	Torrent	444.18	1.9	Indian	Aristo Pharma	1554.71	2.2	Indian
16.	Worckhardt	434.75	1.9	Indian	Dr. Reddys Labs	1436.66	2.0	Indian
17.	Micro Labs	431.67	1.9	Indian	Torrent Pharma	1414.00	2.0	Indian
18.	Novartis	412.07	1.8	MNC	Micro Labs	1307.96	1.8	Indian
19.	Intas	382.41	1.6	Indian	USV	1306.67	1.8	Indian
20.	Unichem	378.91	1.6	Indian	Glenmark	1253.97	1.8	Indian
MNC share in top 20 companies (%)				14.4			21.6	

Note:* Sales value reflects changes in IMS sampling methodology for years under study.

Source: IMS Health.

Annexure Table A-11.3

Therapeutic Segments with High Four-firm Market Concentration (80%-100%) having Market Value greater than ₹ 50 crore

Therapeutic Segments with High Concentration	*Four-Firm Concentration Ratio (CR4)*	*2012 Market Value (₹ in crore)*	*Total MNC Share in Therapeutic Segment*
A10C Human Insulin N Analogues	91%	1240.84	87%
R03C Bronchodil.inhalant Prep.	91%	1054.43	4%
G03K Antiprogestogens	92%	501.71	0%
J07C Toddler Vaccine	93%	418.81	92%
J04A Tuberculostatics Ex	87%	388.30	7%
H03A Thyroid Preparations	96%	316.41	84%
V06C Infant Formulas	99%	284.18	2%
J07B Paediatric Comb.vaccines	91%	279.54	72%
J07A Paediatric Single Vaccine	93%	259.22	47%
D07C Cortico+Antifung.comb.	90%	239.89	62%
A07l Oral Electrolytes	81%	219.15	8%
V03B Ginseng & Rejuvenators	92%	216.39	82%
C02D Alfablockers	91%	152.56	68%
J05A Antivirals Ex.Vaccines	95%	144.67	8%
G02A Oxytocics	85%	139.35	80%
N04A Antiparkinson Drugs	89%	131.41	28%
J06A Sera & Gammaglobulin	95%	127.41	11%
N07C Antivertigo	88%	120.79	69%
A14A Anabolic Hormones	84%	115.29	66%
C01G Potassium Channel Openers	87%	109.97	6%
A11B Multvit. without Minerals	81%	106.07	1%
T02X Other Diagnostic Agents	91%	103.70	16%
J01B Chloramphenicols-Comb.	92%	89.08	63%
A11H Oth. plain Vit.ex.K-P	93%	81.79	76%
A07H Intest.antiinf. Oth.comb.	94%	71.84	1%
N01A Anaesthetics General	82%	68.85	21%
J01E Trimethoprim Comb. & Simi.	93%	64.77	84%
J01H Other Penicillins	98%	63.49	67%
C01B Antiarrhythmics	95%	61.15	88%
S01C Corticoids Plain	81%	53.49	49%

Source: IMS Health.

Annexure Table A-11.4

Therapeutic Segments with Medium Four-firm Market Concentration (50%-80%) having Market Value greater than ₹ 50 crore

Therapeutic Segments with Medium Concentration	*Four-Firm Concentration Ratio (CR4)*	*2012 Market Value (₹ in crore)*	*Total MNC Share in Therapeutic Segment*
R05B Cough Preparations	50%	1950.95	44%
N03A Antiepileptics	68%	1418.89	43%
J01I Quinolones	53%	1176.26	22%
J01F Macrolides and Similar	57%	1017.23	21%
H02A Sys.corticosteroids Pl.	59%	733.58	44%
A12A Calcium Prep.	56%	722.74	29%
A05B Hepatic Prot. lipotropic	54%	710.21	13%
N06A Antidepressant-Thymonal	50%	680.14	21%
A11E Vitamin B Complex	61%	641.03	61%
G03D Progestogen and Simi. comb.	57%	588.89	32%
A02A Antacid-Antiflatulents	66%	560.56	54%
P01D Antimalarials	62%	543.91	8%
M02A Topical Antirheumatics	53%	513.76	49%
A06A Laxatives	58%	512.28	44%
A03C Antispasm. antichol. Comb.	63%	482.81	13%
V06B Protein and Neutr. Suppl.	50%	443.99	29%
B03C Other Anti-Anaemic Prep.	57%	402.37	29%
D07D Cort.+Antifung+Antiinf. co	54%	391.86	43%
N07A Other CNS Drugs	51%	391.59	18%
V03D Drugs for Sexual Disorder	61%	379.01	13%
A01A Stomatologicals	60%	378.34	5%
C02B Ace Inhibitors	67%	363.39	41%
D06A Top. antibiotics Plain	78%	309.03	73%
D08A Antiseptic-Disinfectant	76%	308.27	17%
G03A Hormo. contracep.nontop.	63%	305.81	53%
N05A Antipsychotics	68%	295.47	12%
C03A Diuretics Plain	51%	295.01	32%
G03J Drugs for BPH	77%	292.85	13%

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C01F Nitrates	66%	269.16	35%
V06D Other Nutrients	62%	267.82	62%
L01A Antileukaemics	54%	262.47	32%
S01J Tear Substitute	61%	260.27	50%
B02A Antifibrinolytics	55%	259.09	7%
D02C Demelanizing Agents	69%	246.63	12%
R01A Nasal Decongestants	70%	243.23	57%
J07E Adult Vaccines	71%	241.58	68%
D07B Corticosteroids+Antiinf. C	76%	236.18	71%
K01A Iv So & Electrolytes 50C	73%	236.00	56%
A15A Appetite Stimulants	70%	223.79	7%
A13A Tonics	56%	206.26	12%
D07A Corticosteroids Plain	58%	204.98	46%
N09A Drugs for Alzheimer'disea	65%	200.01	11%
A11C A+D Incl. simple Comb.	54%	194.17	23%
S01G Antiglaucoma	73%	189.62	45%
J01A Tetra and Comb/Doxycyc.	51%	186.59	44%
D01A Antifungal-Dermatological	53%	184.33	35%
J05B Antivirals	68%	162.93	27%
P01B Anthelmintics Ex.Schis.	68%	161.38	49%
G02C Other Gynaeco. prep.	66%	161.31	0%
C01M Other Coronary Vasodilat.	51%	158.03	22%
A11D B1 Plain or with B6-B12	77%	155.59	67%
R03E Bronchodilators Liquids	62%	150.13	6%
D16A Hair Care/Antidandruff P.	55%	143.27	33%
J01M Oxazolidinones	61%	138.33	2%
L04C Immunosuppressive Drugs	54%	137.78	24%
N06C Psycholep.-Psychoanalep.	58%	129.86	11%
A03B Antispasm.antichol. Plain	66%	126.05	30%
N02C Antimigraine Preparations	60%	125.11	22%
A07D Ciprofloxacin Comb.	76%	120.03	38%
A04E Antiemet.-Antinaus Inj.	64%	115.16	5%
D02E Drugs for Alopecia	73%	113.10	6%
M01B Antirheu. Proteolytic Enz.	75%	112.96	5%

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M04A Antigout Preparations	70%	111.08	45%
S02A Otologicals	57%	109.22	22%
S01P Other Ophtha and Ophtha/Oto	52%	106.85	17%
C05C Systemic Vasoprotectives	62%	102.47	17%
P01A Amoebicides	74%	99.87	25%
G03C Oestrogens and Simi. Comb.	73%	96.18	71%
C01P Other Cardiac Prep.	71%	95.11	15%
N05C Hypnotics and Sedatives	79%	94.83	57%
D07E Cort.+ Salicylic Acid	71%	94.05	40%
A07I Intestinal Antiinflammatory	77%	93.80	12%
A04B G.I. Prokinetic	67%	90.70	23%
S01H Nsaid	66%	89.71	39%
A08A Antiobesity Ex. Dietetic	52%	83.52	1%
C04A Peripheral Vasodilator	59%	82.70	34%
A04D Antiemet.-Antinaus Liq.	66%	75.56	2%
A07B Norfloxacin Comb.	75%	74.93	20%
G01B Gynaeco Antiinf. Top.	63%	72.49	8%
D02B Sunscreens	52%	67.97	40%
V01A Allergens	75%	66.92	4%
C05A Top. Antihaemorrhoidals	55%	63.49	25%
R04A Rubs and Balms	72%	51.13	49%
B02B Vitamin K and Others	59%	50.65	7%

Source: IMS Health.

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THIS book discusses in great detail the critical barriers to access to medicines in India despite the country ascending towards the role of 'pharmacy of the global south'. It highlights several themes, considered as impediments to access to medicines while at the same time proposing viable policy options. Some of these themes include inadequate investment in public health care, inefficient and unreliable procurement and distribution of drugs, unaffordable drug prices and pharmaceutical patents. The book calls for scaling up investment and to replicate the success of a 'centralised procurement and decentralised distribution' model of drugs, as in the state of Tamil Nadu, which will pave the way for universal access to essential medicines in India.

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